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ASBESTOS AND CANCER

THE FIRST THIRTY YEARS

by

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with the assistance of

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PREFACE

In the Spring of 1976 I was asked by the Asbestos Information Association if I might have a student or students who, under my direction, could do a literature review for the purpose of preparing a history of the development of knowledge about the health effects of asbestos. The idea was to determine how, at different points in time, the medical profession interpreted the research literature then available to it. I saw an important area for research here in regard to the relationship between asbestos and cancer. This had been an area of interest to me since 1961 when I first became involved with occupational health. At that time I joined the Division of Occupational Health of the U. S. Public Health Service — a predecessor of the present National Institute of Occupational Safety and Health. One of the first tasks given to me was to develop epidemiological data with regard to any relationship between asbestos dust exposure and lung cancer in the United States. The basis for this was an internal document that reviewed the literature and posed the question, "Does asbestosis predispose to lung cancer?"* I assumed at that time that this was an important but unanswered question. Since then, many of my colleagues have indicated to me that this issue was settled long before 1961. I, therefore, welcomed the opportunity to carry out a project aimed at seeing what were the attitudes and opinions about this and when, in fact, did the debate really end. I was fairly sure this was no later than 1964 when an international meeting was held in New York City on the biological effects of asbestos in which I participated.

*"Ad hoc meeting to discuss the status of knowledge concerning the effects of exposure to asbestos dust on health" for internal distribution only, May 19, 1961.

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The project was carried out in three stages. First, two of my students collected and read all of the literature referenced in the Index Medicus and elsewhere for the years 1934-1965. This included building on references in each article found. In addition, they examined every issue of Lancet, the British Medical Journal, and the Journal of the American Medical Association for these years for any editorials or communications which mentioned asbestos and cancer. Also, all available textbooks on occupational medicine, toxicology, or pulmonary cancer were examined. An abstract of each article was prepared and where attitudes were expressed on the question of does asbestos cause cancer, that section of the article was zeroxed for subsequent study. The Asbestos Information Association had all foreign language articles translated in their entirety.

The second stage included classifying each article or writing as to whether the author thought asbestos definitely caused cancer, possibly caused cancer, or felt the issue was unproven, or that asbestos did not cause cancer. This was done separately for lung cancer and for mesothelioma. For lung cancer, an additional classification was made for those writers who believed asbestos definitely or possibly caused lung cancer as to whether they believed asbestosis was or was not a prerequisite. This classification was made independently by two reviewers, using the zeroxed sheets prepared by my student assistants and by reading the entire article where necessary. There were surprisingly few disagreements. These were worked out by discussion, and in some cases, by compromise.

In the third stage, I prepared a narrative literature review in which I tried to link the literature together, seeing who was quoting who, who was given credit for discovering the relationship between asbestos and cancer, what articles and reports stimulated others, and tracing individual writers'

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attitudes and opinions over time. In this, I tried not to evaluate the data presented or criticize what was said about it, since my objective was to see what people thought about what they were seeing at the time, rather than what I saw in the data. Neither did I try to judge the writers, either in terms of their technical or professional competences or any biases or motives they might have had. I did at times comment, however, on their knowledge of the literature. While my major focus was on asbestos and lung cancer, by 1960 I found I could not ignore the mounting volume of literature on asbestos and mesotheliomas and, at that point, I briefly summarized what had gone before and included subsequent writings on mesothelioma in my narrative. In addition, I addressed directly the question of when was the relationship between asbestos and cancer actually accepted in the United States. This represents only my own view. Obviously, my feelings about the role epidemiologic observations played in the acceptance of a relationship is a central issue here.

Among the things I gained from this research was a deep respect for the clinicians and pathologists who contributed to the early literature. They showed remarkable insight into the meaning of their observations, and the logic of their conclusions was far more reasoned than I had expected. I also became far less sure that the sharp distinction made by many writers between epidemiological as contrasted with clinical-pathological observation served a useful purpose. Even a single case report is a kind of epidemiologic observation, since the basis of such reports is usually a feeling, unexpressed, that the case is somehow aberrant for a human population.

I express my deep appreciation to Ms. Nancy Sussman and Dr. Gary Marsh who assisted me in this project, not only in locating and abstracting the literature, but in reviewing and challenging my interpretation, to Dr. Ian Higgins, who independently classified the literature with regard to opinions of authors

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on the relationship between asbestos and lung cancer, and who also pointed out to me what the clinicians and pathologists were really seeing in their case reports, and why these constituted in their minds important evidence—evidence often ignored by biostatisticians. Dr. Higgins knew many of the writers on asbestos and cancer in the period 1934-65, was a student of W. Burton Wood, and personally knew S. Roadhouse Gloyne. I am also grateful to Ms. Mary Doninar and Ms. Catherine Brosky, librarians at the Graduate School of Public Health of the University of Pittsburgh, who miraculously produced nearly every piece of literature referenced here. I am particularly appreciative of the efforts of Ms. Shirley Duff, who patiently typed and edited a succession of drafts of this manuscript. I express my appreciation to the Asbestos Information Association who provided financial support with the understanding that information regarding the development of knowledge about asbestos and cancer might seriously weaken the asbestos industry's position in litigations against it. Finally, I acknowledge the contribution of the University of Pittsburgh who largely underwrote my efforts by granting me a sabbatical leave during which much of my work on this project was carried out.

Philip E. Enterline
Pittsburgh, PA
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THE LITERATURE, 1934-64

1 -World War II

In 1934 W. Burton Wood and S. Roadhouse Gloyne reported on two cases of carcinoma of the lung among 53 cases of asbestosis. Gloyne had been interested in the effects of inhalation of asbestos dust starting in 1928, when he first observed cases of asbestosis from an asbestos plant near London attending a chest clinic or seen at autopsy. In 1933 he published a report on a series of asbestosis cases and noted one abdominal carcinoma and one squamous carcinoma of the pleura. At that time he stated that, "There is no evidence at the moment that this [the cancer] is in any way related to asbestosis." In his 1934 report he did not discuss the possibility that cancer might be related to asbestosis. His primary interest, and the interest of many writers at that time, was in tuberculosis as it related to asbestosis. As for the future in regard to asbestosis, he was optimistic stating that:

> "The picture of pulmonary asbestosis is that of a pneumoconiosis occurring in a factory in which few precautions have been taken to protect the workers from a danger, the gravity of which was not realized. Happily, these conditions are now a thing of the past, and elaborate precautions have been taken to protect the worker."

Gloyne was referring to the Asbestos Industries Regulations of 1931, which reduced dust levels in asbestos factories.

In 1935 Gloyne reported in detail on the two lung cancers in asbestosis cases in his report with Wood in 1934. In neither case was the malignancy recognized until autopsy. Both were women workers in an asbestos plant — one a spinner and the other in the mattress and opening department of the factory. This time he considered a causal relationship quoting Bridge and Henry (1928) on two conditions required for classifying cancer as industrial in origin: "(1) that the incidence rate in the occupation under review should

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exceed that in the general population, to a significant extent and (2) that in the occupation concerned, there should be sufficient association of the worker with a substance proved experimentally to have carcinogenic properties." He was unconvinced of a relationship, although he was aware of and referenced a report from the United States by Lynch and Smith (1935) in which a possible relationship was considered. Gloyne stated, "It seems worthwhile ... to record the two cases, not in any attempt to make out an aetological association of these two diseases, but in order to emphasize certain histological points in which one disease appears to bear upon the other."

Generally, credit for recognizing a relationship between asbestosis and lung cancer is given to Lynch and Smith who earlier in 1935 reported on a single case as "worthy of record in the interest of both diseases, as well as their possible relationship ..." This case was a man who worked as a weaver at an asbestos factory for 21 years "in an extremely dusty atmosphere in spite of the fact that windows and doors were kept open as much as possible." Lynch and Smith subscribed to "a conception of its origin [lung cancer] by reason of chronic bronchial irritation ..." and felt this was "comparable with the current knowledge of the etiology of such tumors." They were apparently unaware of Wood and Gloyne's report in 1934.

In 1936 Egbert and Geiger reported on a single case of lung cancer in association with asbestosis which they "deemed especially interesting since it is apparently the first to describe primary carcinoma of the lung as an associated condition." They also refer to an earlier article by Egbert (1935) in which "pulmonary tuberculosis was found to be a common complicating condition," and refer to reports of other forms of pneumoconiosis in which carcinoma of the lung has occurred. Moreover, they attributed the 10 percent incidence of carcinoma of the lung found at autopsy among cobalt

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miners at Schneeberg to pneumoconiosis.* They are the first of many writers to consider pneumoconiosis generically and reason that if asbestosis is related to cancer, so then must silicosis and other pneumoconioses. In December of 1936, Gloyne reported on an additional lung cancer in a case of asbestosis, but without comment as to any causal relationship beyond the statement that it "appears to be worth recording."

In 1938, a book on silicosis and asbestosis was published by Lanza. One chapter was prepared by Gloyne. In this, Gloyne stated that, "No definite conclusion can be drawn on the relation between these two diseases [asbestosis and pulmonary cancer] until more material is available." Gloyne interpreted his data with much caution. It was 13 years before he published again on the subject of asbestosis and cancer. Also in 1938, a man of strong conviction emerged. Martin Nordmann, writing in German, observed two cases of lung cancer in two cases of asbestosis at autopsy. He presented these plus a review of the case reported by Lynch and Smith (1935), the two cases reported by Wood and Gloyne (1934) and the case reported by Egbert and Geiger (1936). He concluded that "a cause-effect correlation must be present here, even if I had been the only observer" and concluded "we are indeed facing an occupational cancer which affects asbestos workers." Nordmann felt this had "far-reaching significance ... for our insurance system." Interestingly, Nordmann also accepted the relationship of asbestosis to tuberculosis reported by Egbert and Geiger, and reported by Wood and Gloyne. On the other hand, he rejected the notion that all the pneumoconioses are related to lung cancer, pointing out that asbestos must contain some carcinogenic substance — like arsenic or radioactivity.

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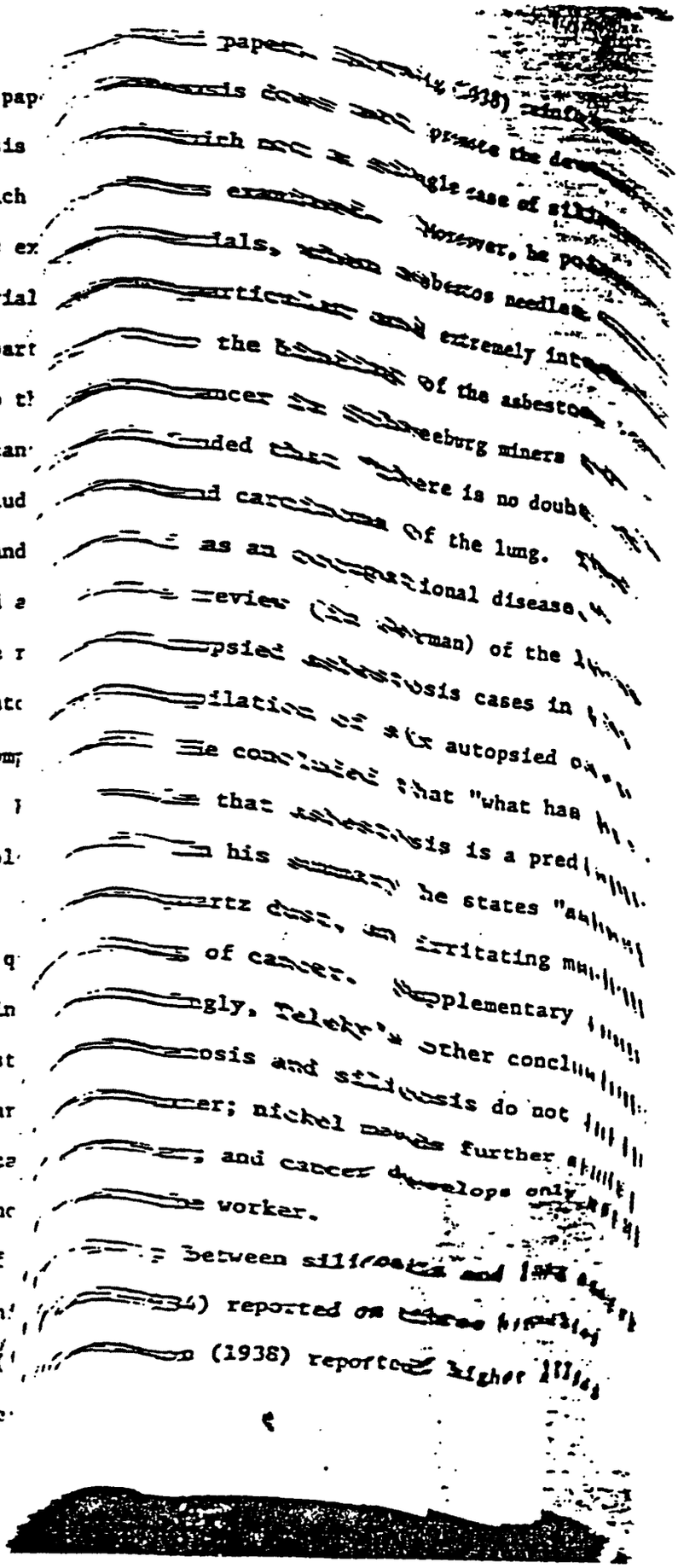
*The possibility of industrially-induced lung cancer had been demonstrated as early as 1879 among cobalt miners of the Schneeberg district in Saxony, Germany. Harper (1942) gives an excellent account of this. The Schneeberg experience was well known in 1936.

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In a simultaneously published pap
(tion that, unlike asbestosis, silicosis
carcinoma and referred to a study in which
carcinoma occurred in 186 stonecutters ex
that "unlike silicosis-producing material
contact with the body fluids a very part
reaction occurs which finally leads to t
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content in the lungs of lung cancer cases than in a series of controls, and concluded that silicosis was etiological in pulmonary carcinoma. By contrast, Vorwald and Karr (1938) collected all the published roentgenological and autopsy reports on pneumoconiosis along with a smaller series of their own and concluded that inhaled dust was not of etiological significance in the development of primary pulmonary carcinoma. They supplemented this review with an experiment involving 3,338 animals exposed to many different kinds of dust for long periods of time. Only two animals revealed the presence of pulmonary neoplasm. Included in the experiment were 235 guinea pigs exposed to asbestos, none of which developed pulmonary neoplasms. While Vorwald and Karr do not comment on asbestos, reading of their material leaves the impression that asbestosis is no different from the other pneumoconioses. They state that, except for the two pulmonary neoplasms, all animals "failed to show evident initiation, hyperplasia or tumor transformation of the epithelium lining of the respiratory passages" and "this was observed irrespective of the activity of the dust, whether it was inert or had caused marked fibrosis of the pulmonary tissue." Vorwald and Karr's article was the subject of an editorial comment in the Journal of the American Medical Association (1938). In this, emphasis was placed on the noncarcinogenic nature of industrial dust unless such dust contained recognized carcinogenic substances. The comprehensiveness of Vorwald and Karr's review, coupled with their animal experimental data, made this an important article and strongly suggested that asbestos dust was not carcinogenic.

The entire situation was also commented on in an editorial in the British Medical Journal in August of 1938. The conclusions by Dible and Anderson that silicosis predisposed to bronchial carcinoma was questioned, and Vorwald and Karr's data, along with a study by Kennaway and Kennaway

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(1936), were presented as evidence against an association between pneumoconiosis and cancer.* Nordmann's article on asbestosis and lung cancer was noted with the comment that "... the recorded instances are as yet too few to be significant." In 1939, the International Labour Office issued a report on occupation and health. They list eight cases of associated lung cancer and asbestosis in the world literature and conclude that "the cases are too few to be of any value."

By the end of 1938, attitudes and opinions about asbestos and lung cancer had begun to form along nationalistic lines. The Americans and the Germans largely settled in extreme positions with the Germans holding to the views of Nordmann (1938), and the Americans continuing to argue the issue of silicosis and cancer and pointedly ignoring the early suggestion of an association with asbestosis by Lynch and Smith (1935). The British became silent on the issue, with no further published reports or opinions until 1946. Interchange of scientific literature between Germany and the Allies must have been limited during this period. It seems instructive at this point to look at the German literature for the period 1939-45 and then compare this with the U.S. and Canadian literature for the same period.

The German Literature 1939-45

In 1939, Baader in a lecture to the Berlin Medical Society referred to Nordmann's work and reports of combined asbestosis and lung cancer in the literature, and concluded that "there is unfortunately no longer any doubt that lung cancer is the occupational cancer of the asbestos workers." Also, in 1939, Saupe reported on chest X-rays of 420 asbestos workers on which no

*In 1936 Kennaway and Kennaway reported on a study of 18,280 death certificates which showed cancer of the lung or larynx in England and Wales from 1921 to 1932. Not one of these was an asbestos worker.

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lung cancer or tuberculosis was detected. While Saupe felt that this demonstrated a lack of association between asbestos and tuberculosis, he did not feel that his findings conflicted with Nordmann's conclusions about asbestosis and cancer, pointing out that his subjects were too young for "such cancers."

In 1941, Nordmann and Sorge reported on 100 white mice exposed to a dense cloud of asbestos dust for 6-13 weeks. Two pulmonary carcinomas were observed — the earliest after 240 days. Since only 10 of the 100 mice survived to 240 days, they calculated the percentage response as 2 out of 10 or 20%. They felt this provided "experimental support of the causal significance for primary lung carcinoma in asbestos workers." Linzbach and Wedler (1941) described a severe case of asbestosis of the lungs in a 60 year old man who developed a squamous cell epithelial carcinoma in the right inferior lobe. They concluded that "the cause of carcinogenesis is to be found in the damage caused by asbestos, and this cancer must be classified as occupational, as proposed by Nordmann."

In 1942, Wegelin wrote on the etiology of lung cancer. He did not feel there was a relationship between silicosis and lung cancer but felt the situation was "somewhat different in the case of asbestosis, which lends to a high percentage of pulmonary cancer, according to Nordmann in 12 to 20 percent of asbestos workers." He also referred to the findings of Nordmann and Sorge on mice to support his position. In the same year, Welz also referred to Nordmann's work and indicated that, at a meeting of the German committee on asbestosis in Dresden, Nordmann reported on eleven cancer cases in asbestosis patients (as compared with six in his original 1939 articles). He also stated that "representatives of the German trade association agreed (at the Dresden meeting) with Nordmann's theory and recognized lung cancer ... as an occupational disease." Welz also complained that "researchers in

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America and England were reluctant to agree with the alleged significance of asbestos dust for the development of primary carcinoma."

In 1943, Wedler continued along the same line as earlier German writers. At this point, German articles give credit for the discovery of the relationship between asbestosis and cancer to Nordmann. Wedler states that "all the observations up to now tend to indicate with all probability that Nordmann's theory on occupational cancer in asbestos workers is a valid one." He went on to say that "no specialist in Germany has ever adopted a different stand on this matter." In another article in the same year, Wedler states that "the association with pulmonary tuberculosis is much more rare than that observed in the case of silicosis" and that "asbestos shows no noteworthy influence on the frequency and course of tuberculosis of the lung." Boemke (1943) agreed with other German writers on the subject of lung cancer and asbestosis and stated, "Nordmann was the first to suggest a relationship between asbestosis and lung carcinoma." He also notes that "publications in the foreign literature maintain reservations with regards to any possible correlation of the origin of these two diseases."

Nothing was published in German on the subject of asbestos and lung cancer in 1944 and 1945. The position of the Germans was clear, however: asbestos causes lung cancer, but not tuberculosis; silicosis does not cause lung cancer; and Nordmann discovered the relationship between asbestosis and lung cancer.

The American and Canadian Literature 1939-45

In the North American literature, there was a preoccupation with the subject of silicosis and lung cancer. In 1939, Lanza and Goldberg published text on industrial hygiene. In their chapter on silicosis and asbestosis, they note that cancer, cardio-vascular disease, nephritis and tuberculosis

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sometimes occur with asbestosis but indicate that "it is difficult to assess the role of asbestosis in these cases." Klotz (1939) did an autopsy survey on 50 silicotics in Canada and found four cases of lung cancer. He reviewed the literature as of that date and concluded that "in the main the tendency is to support the contention that silicosis or other forms of pneumoconiosis may play a part in the production of primary carcinoma of the lung" and felt that his own data "indicate that silicosis may be a definite predisposing factor in the development of carcinoma of the lung." Also in 1939, Lynch and Smith again reported a case of lung cancer in an asbestos weaver with asbestosi: In addition, they reported on 2,343 consecutive autopsies during the previous 12 years. Of these, 35 showed some degree of asbestosis and in 2 of these, lung cancer was also present. This incidence of approximately 6 percent compared with an incidence of 0.3 percent in their necropsy service. Their conclusions were guarded, however. "Whether this is to be taken as of significance, especially in comparison to the general rate, is questionable. The series of asbestosis cases is small and the possibility of statistical error great."

In 1940 Gardner reviewed the problem of pneumoconiosis. Some of his review was devoted to the possibility that asbestosis predisposed to tuberculosis. He concluded that "tuberculosis may be an unusually frequent cause of death in certain groups of asbestos workers, but at present it seems more probable that nonspecific hygenic factors and general living conditions are responsible." He went on to note that "the actual frequency of nontuberculosis infection and primary cancer of the lungs are unknown. One must not be misled by the comparatively small number of postmortem reports."

In 1941 Desmeules, a French Canadian writing in French, reported on two cases of lung cancer in a machine fitter and an asbestos bagger with

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asbestosis. He concluded that "we consider it logical that, as has been assumed for silicosis, asbestosis may represent a predisposing factor for pulmonary carcinoma." Desmeules, incidentally, seemed to be unaware of much literature on the subject, referencing only the 1936 article by Egbert and Geiger.

In 1942, Holleb and Angrist reported on two cases of lung cancer in pipe coverers (using asbestos fabric) with asbestosis. They updated Nordmann tabular presentation of six cases by adding four additional cases. They were reluctant to agree with Nordmann, however, pointing out that "these data are presented as a summary and not necessarily as supportive evidence for Nordman conclusions." Holleb and Angrist also refer to the chapter Gloyne prepared for the textbook by Lanza, in which he stated that, "No definite conclusion can be drawn on the relation between these two diseases [asbestosis and pulmonary cancer] until more material is available."

A textbook on occupational medicine was published by Wampler in 1943. Asbestosis was described as a consequence of asbestos dust exposure, but no mention was made of cancer. It seems likely that if Wampler believed an association existed or was a strong possibility, he would have so noted. In any event, readers of his text interested in asbestos could gain no clue as to the literature in this field. In 1943, Homberger reported three lung cancer cases in association with asbestosis, and in addition reviewed the literature on the association of pulmonary asbestosis and carcinoma. None of the German literature published after Linzbach and Wedler's article in 1941 was referenced In his own series of cases, he reported "the association of the two conditions is remarkably high. In 8 cases of asbestosis, there were 4 instances of primary pulmonary carcinoma." In his discussion, however, he concludes, "These facts seem to indicate that [illegible]

purely morphologic studies is there any reliable answer to the question of whether pulmonary asbestosis has to be considered as an etiologic factor in pulmonary carcinoma."

The first of many publications on asbestosis and lung cancer by Hueper appeared in 1942. This was the earliest book devoted solely to occupational cancer, and it it Hueper dealt with a wide variety of proven or possible occupational carcinogens. He reviewed the world literature on asbestosis and cancer and concluded that "an evaluation of the evidence presented reveals certain features connected with these cases which are suggestive of an occupational cancer." He felt there were three arguments in favor of an association (a) the incidence of lung cancer in asbestosis of the lung is definitely excessive, (b) the young age of an appreciable number of cases thus far recorded and a relationship between the time of exposure to asbestos dust and manifestations of neoplasms throughout the entire series, and (c) a shift in histological types in the direction of a predominance of cancroids, and in the multicentric development of two and possibly even three of the cases he reviewed. He felt that the small number of asbestosis carcinomas of the lung "did not disprove an occupational origin" and that experience with other industrial neoplasms "has shown that such isolated cases may represent the first warning of a subsequent appearance of large numbers of similar tumors of undeniable occupational deviation." Hueper also published a review and discussion of occupational cancer in 1943. Now he is sure. He stated that, "Asbestosis cancer of the lung is the most recent newcomer among the occupational cancers of this organ. First described in 1935, there are now 18 cases of this industrial cancer on record observed among asbestos workers in England, Germany, and the United States."

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Hueper clearly reflected the position of the Germans with regard to asbestosis and lung cancer, and the German literature was probably easily known to him since he was German born and educated. Hueper was the first American to come out definitely in favor of the association.*

By the end of World War II, an association between asbestos and lung cancer was well recognized in Germany, but not generally accepted elsewhere. Nordmann had developed a large following, whereas no strong figure emerged in England or America. Gloyne, and Lynch and Smith, whose work appeared well ahead of Nordmann's, were cautious in their views and remained unconvinced. The medical profession and the asbestos industry in England and America had good reason to be complacent.

The Post World War II Period

1946

Fleischer, Giles, Gade and Drucker reported on X-ray examinations of 1,074 pipe coverers using asbestos. No cancers were observed and only three cases of asbestosis were found. They stated that "... it may be concluded that such pipe covering is not a dangerous occupation." Hueper restated his views on asbestosis and cancer in two separate articles. Also, an experimental study on 40 rabbits was reported by King, Clegg, and Rae, and no cancer was observed after intertracheal administration of asbestos.

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*Hueper also listed the following occupational exposures as carcinogenic: arsenic, chromates, nickel carbonyl, radium, mesothorium, asbestos, crude mineral oil, pitch, tar, soot, paraffin oil, anthrocene oil, creosote, aromatic amine compounds, benzol, ultra violet rays, roentgen-rays and rays of radioactive substances, and certain parasitic worms. He suspected iron, lead and nitrates. He attributed tobacco smoking to cancer of the mouth, lips, and cheeks.

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1947

Writing in Finnish, Wegelius reported on an X-ray survey of 476 workers from an asbestos mine and from an asbestos factory. One hundred twenty-six were found with asbestosis but "not a single case of carcinoma." Kennaway and Kennaway reported on the relationship between cancer of the lung or larynx and various occupations as recorded on death certificates in the years 1934-38. They found eight cases of cancer of the lung in male asbestos workers in England aged 45 to 65. They calculated that if the rate in the general population prevailed for asbestos workers, these 8 cases would need to have come from a population of 4,000 asbestos workers. They state, "The number of male asbestos workers in this age group appears to be considerably less than 4,000 but, as we have been unable to obtain any exact information for the workers at risk, one cannot carry the calculation further." Elsewhere in their study, they examined the incidence of lung cancer in occupations with liability to silicosis. They quoted Dible, Anderson and Dible, and Klotz who, along with their data, seem to support the notion that silicosis predisposes to lung cancer. Thus, once again, the question of whether all pneumoconioses might be a factor in lung cancer was raised.

1948

Cureton reported on a squamous cell carcinoma in an asbestotic worker from a factory making asbestos pipe covering. He stated in his commentary that, "Literature review regarding the association between asbestos and the development of neoplasms leaves the question still open." On the other hand, he discusses his own case as though it was indeed caused by asbestos, discussing the latent period and exposure duration.

The first paper in Italian (Saita) appeared. The author reviewed the evidence, quoting extensively from Nordmann. In Italy no cases of pulmonary

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(mors in subjects with asbestosis had been described at that time. He concluded, however, "that the data from the foreign literature are so suggestive that they do not leave many doubts concerning the facility of finding asbestosis with pulmonary cancer." He went on to say "... only asbestos dust and coal tar derivatives possess an undoubted carcinogenic effect on the lungs." This was not very reassuring in view of the much referenced Schneeburg miners experience. Saita also reviewed evidence for an association of silicosis with cancer and concludes that there was probably no relationship.

Lynch reported on asbestosis and lung cancer at a meeting of the American College of Chest Physicians in June, 1948, and published a paper with Cannon. They reviewed 40 cases of asbestosis seen over a period of 18 years in which 3 cases of lung cancer were found. Interestingly, they treated asbestosis and silicosis together in their discussion, making no distinction between the two with regard to the question of cancer. Lynch continued to be cautious, concluding that, "From the reports of the natural occurrence and from the question raised by experimental evidence, it seems that continued effort, especially experimental, should be made to evaluate this important problem. In a discussion of this paper, Brahdy seemed a little annoyed that Lynch remained skeptical stating, "Although we must keep an open mind, the evidence warrants the tentative conclusion that asbestos workers do have a higher incidence of cancer."

Earlier in 1948, in a paper read at the Symposium on Occupational Cancer at the Eighth Congress on Industrial Health, Warren was cautious about the relationship, "It is well to remember that the mere occurrence of a tumor in conjunction with a recognized occupational disease may be fortuitous, as in the case of cancer of the bronchus in a person already suffering from asbestosis." Warren argued that in occupational tumors, an abnormal state

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of tissues existed for an appreciable period before the lesion became cancerous, using as an illustration epidermal carcinoma of the skin following irradiation injury, and the fact that chronic roentgen ray dermatitis long antidates the development of cancer.

Teleky, who had first reviewed the situation on the relationship between asbestosis and cancer in 1938, wrote a book dealing with the history of factory and mine hygiene and this time published in English (his earlier work was in German). Curiously, while he discussed asbestosis in some detail, he did not mention any relationship to cancer.

An important textbook on occupational medicine by Johnstone appeared. While asbestosis was described, cancer was not mentioned in association with the disease. This book does discuss differences between asbestos and silica, however, and quotes Gardiner: "... inhaled asbestos fibers are irritating not because they are silicates but because they are stiff fibers which mechanically irritate the lungs." Johnstone also believed that short fibers (< 2 μg) were not dangerous, referring to a lack of asbestosis among workers at Thetford Mills (apparently Thetford Mines in Quebec, Canada). He mentioned animal work in support of the notion that short fibers are safe.

1949

Since asbestosis was a compensable disease in England and Wales, the numbers of cases were routinely reported in the Annual Report of the Chief Inspector of Factories. In their 1947 paper, Kennaway and Kennaway referred to these and, in particular, to the report for 1938 which listed 103 fatal cases of asbestosis during the period 1932-38. That report also presented the number of lung cancers among fatal asbestosis cases. Kennaway and Kennaway found these data difficult to evaluate since there was no control series, and they were not sure the proportion of lung cancer cases was definitely higher than might be expected in other diseases.

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In 1949, Merewether, then Chief Inspector of Factories, provided an answer to this question. In his report for 1947 (actually published in 1949), Merewether provided data on lung cancer in both fatal cases of asbestosis and in fatal cases of silicosis. In 235 deaths either caused by asbestosis or in which asbestosis was proved at autopsy, cancer of the lung or pleura was found in 31 or 13.2%. For comparison, he analyzed 6,884 cases of silicosis occurring between 1930 and 1946. Only ninety-one of these, or 1.3% were found to have cancer of the lung or pleura at postmortem.

Merewether's data did not go unnoticed. The Journal of the American Medical Association in an editorial reported fully on Merewether's findings, adding the observation that there was a distinct shift in the sex distribution of lung cancer in his series. "The male-female sex ratio is 2.4:1, while it is 5:1 for cancers of the lung in general." This was the first time any notice was given of the relatively high proportion of females among asbestosis-cancer cases, although in Gloyne's 1935 report both cases were females. The JAMA editorial also referenced work by Wedler and by Nordmann and Sorge, and was strongly supportive of an association: "As the available evidence shows, the occurrence of cancer of the lung is related to pulmonary asbestosis and is not merely a possible sequela of exposure to asbestos dust. In all fatal cases of asbestosis there should be postmortem examination with detailed histologic analysis."

Other articles which appeared in 1949 also referenced Merewether's report. Wyers reported 17 cases of lung cancer and 7 cases of cancer of other organs among 115 autopsied cases of asbestosis, and referenced Merewether, Wedler, and Boemke in support of an association. Doig, in a discussion of dust-caused diseases, dispelled the notion that silica played an etiologic part in producing malignant disease, using the data of Merewether.

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L. W. Smith, also in a review and discussion, referred to Merewether's report under the heading "Incidence Establishes Relationship." He also referred to the cautious conclusions by Lynch and Smith, and Holleb and Angrist, to the strong views of Nordmann and Wedler, and to the 1949 JAMA editorial. Smith states in his introduction that, "More and more evidence appears to be accumulating to incriminate asbestosis in this connection." He seems to accept the relationship based on Merewether's data and the JAMA editorial.

1950

No reports on asbestos and lung cancer appeared in 1950.

1951

Anyone interested in industrial hazards in 1951 might have consulted a "Handbook of Dangerous Materials" by Sax. He would have found asbestos listed as a cause of asbestosis, but no mention of cancer. Hueper, however, again reviewed the matter of asbestos and cancer. He reiterated the views he expressed in 1943, now quoting extensively from Merewether. Hueper acknowledged Warren's 1948 paper but dismissed his conclusion that the association between asbestosis and lung cancer is of coincidental nature, stating that "... the actual existence of a relationship appears to be very likely."

Other writers who believed in an association were Stoll, Bass, and Angrist. They reported on a case in an asbestos pipe coverer and favored the belief that the silicate in asbestos is directly carcinogenic. They clearly accepted the association between asbestosis and cancer, however. Owen also reported a case of asbestosis and lung cancer at autopsy in a worker from an asbestos factory. While no personal opinion is given, there is a personal communication from Professor M. L. Stewart who states that he is "satisfied that there is a statistical relationship between silicosis and asbestosis and cancer, and particularly with the squamous type."

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After a 13-year silence on the subject of asbestosis and cancer, a paper by Gloyne was published posthumously in 1951. In this paper he reported on examinations of 1,205 lungs or parts of lungs of workers exposed to dust. Among these, pneumoconiosis was present in 1,036. For lungs showing silicosis, 6.9% had a primary neoplasm of the lung; for lungs showing asbestosis, 14.1%; and for other types of pneumoconiosis, 6.7%. Gloyne noted that "selection is obviously at work in picking out these cases for special observations..." and pointed out that the necropsy records at the London Chest Hospital show 21.3% primary lung cancer, whereas the Register General reported that for 1948, 2.4% of deaths from all causes in the general population over the age of 15 were due to malignant disease of the lung. He remained cautious with regards to the association of pneumoconiosis with lung cancer but did state that "... the mortality of asbestos workers is disturbing." He went on to say: "This is all the more striking because many of these were females (41.2%). This proportion of female deaths is greater than that in the general population, where the incidence of primary cancer of the lung is 4.4 males to 1 female."

Two experimental animal studies were reported in 1951 -- both negative. Vorwald, Durkan and Pratt exposed various species of animals by inhalation or intertracheal injection of long chrysotile asbestos fibers and did not report any lung tumors. Behrens injected asbestos interperitoneally and intratracheally in rats and mice and did not report any tumors.

One interesting piece of information was reported in the American literature by Tabershaw. In West Germany, asbestosis (of any degree) when associated with cancer of the lung had been declared an occupational disease.*

*Ordinance dated April 27, 1950.

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Starting with the paper by Nordmann (1938), the Germans were unshaken in their belief that asbestos was a cause of occupational lung cancer. Perhaps it would have been officially recognized at a much earlier date had not the war intervened.

1952

Two papers appeared by W. E. Smith. One of these was actually an address given at a meeting of the Cancer Prevention Committee in New York three years earlier (in 1949). In this he reviewed animal work with asbestos and pointed out that the "experience described by Nordmann and Sorge (1941) does not afford evidence that asbestos dust is capable of provoking tumors. On the contrary, it would appear to demonstrate that asbestos dust did not provoke lung tumors under the conditions of the test employed." According to Smith, of the two tumors in asbestos exposed rats, one was, based on the photographs presented, a mere squamous cell metaplasia while the other, asserted to be an adenocarcinoma, "is a type of tumor that can arise spontaneously from the mouse adenoma." This interpretation of Nordmann and Sorge's data, coupled with apparently negative experimental data by Vorwald (1938), King (1946), Vorwald (1951), and Behrens (1951) seemed to seriously weaken the case against asbestos as a carcinogen.

Smith also published a delightful paper in which he recounted his findings on a trip to Europe. He begins this report: "On June 28, 1950, I sailed from New York with the object of visiting individuals engaged in the study of occupational tumor problems abroad." He visited Merewether, Gloyne [illegible], and Wyers in England with regard to asbestosis and cancer and reported: "It was the concensus of [Gloyne, Wyers and Merewether] that a lung tumor hazard formerly existed in this industry [the asbestos industry] in Great Britain but that there is no evidence to show that such a hazard

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continues to exist under the working conditions now prevailing." Following this paper, there is a discussion in which A. L. Lanza casts doubt on the English claims for an association between asbestosis and lung cancer since it was based on lungs that a pathologist searched with a microscope, and he wondered how many cases of lung cancer would be found if lungs from any sort of populations were subject to the same minute scrutiny. These remarks reinforced a discussion by Paul Cartier, from the Thetford Industrial Clinic at Thetford Mines, Quebec, the largest center for mining asbestos in North America. Dr. Cartier reported on eight cases of primary cancer of the lung detected among 4,000 asbestos workers from 1940 to 1950. He felt that the variety of tumors did not support an association since it would be logical to assume that "the same causal factors will produce the same type of tumor." In this discussion, doubt was also cast on the likelihood of an association E. A. Lew, a statistician for the Metropolitan Life Insurance Company, who pointed to possible lack of statistical significance.

Hueper wrote again on environmental cancers in 1952, reviewing the literature, identifying 60 cases of asbestosis and cancer on record, and pointing to the large number of females in this series and a shift toward younger ages for cancers associated with asbestosis. He also introduced the notion that high levels of asbestos dust exposure may cause individuals to die of asbestosis before lung cancer could develop. As of 1952, he notes that Lanza, Vorwald, Warren, and Cartier are quite skeptical about the relationship. Cureton and Homberger are undecided, while Kennaway, Merewether, Teleky, Nordmann, Hueper, Gross, Lecour, Smith, Saita, Wegelin, Linzbach and Wedler, Stoll, Enss and Angrist, and Welz accept the relationship or consider it to be highly probable. Hueper clearly believed that asbestosis was essential for the development of lung cancer — if only as an indication of the intense

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exposure needed for the development of lung cancer. However, he acknowledged the equivocal results of animal experiments and felt the work by Nordmann and Sorge (1941) needed to be confirmed.

Two articles in German appeared. One by Werber reported a lung cancer case in the owner of an asbestos plant. He reported that this case met German requirements for an occupational disease. The other was a review by Behrens who, interestingly, gives credit for the discovery of the relationship to Wood and Gloyne.* Both German writers subscribe to a causal relationship between asbestosis and lung cancer.

1953

Two articles in German also appeared in 1953. Weiss reported on a cancer of the pleura in a worker at a naval dockyard insulating pipes and valve systems with asbestos. He had no doubt that asbestosis and lung cancer are related and felt that pleural cancer is a special form of occupational cancer of asbestos workers. This patient "received indemnity for an occupational disease." Weiss joined most other German writers in crediting Nordmann with discovery that "lung cancer is an occupational disease of asbestos workers." Boemke reported on three lung cancers in three asbestosis cases (autopsy) and speaks of the "undisputable correlation." He also noted the location of these cancers in the lower lobes, a point not emphasized by other writers.**

An interesting thing happened in 1953. Isselbacher, Klaus, and Hardy linked cigarette smoking to lung cancer in an asbestos worker. In a

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*Other German writers gave credit to Nordmann.

**Five of the six cancers listed by Nordmann in 1938 were in the lower lobes, however, he did not comment on this.

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whether asbestosis may play an etiologic role in the occurrence of carcinoma of the lung is not conclusive but that it does support the suspicion sufficiently to require investigation ..."

1954

No reports on asbestosis and pulmonary cancer appeared in 1954.*

Status at the End of 1954

1954 marked the end of a period in which clinical-pathological observations were largely the basis for conclusion. At this point in time, outside of Germany, there appeared to be no clear concensus — particularly among American writers. Cancer had not been induced experimentally, except by Nordmann, and Smith and even Hueper expressed some doubts about these data. Probably more important, leaders in the field of occupational diseases, Lanza, Vorwald, and Gardner remained skeptical. The writers to whom credit for the discovery for a relationship should have gone: Gloyne in England and Lynch in America, had remained cautious. The notion suggested by Smith, that it might even be true in England but not in America, provided reinforcement for those who were reluctant to believe. Probably most revealing was the published discussion of W. E. Smith's 1952 paper on the findings as the result of his trip to Europe. Cartier probably had seen more asbestos exposed workers in his clinic at Thetford Mines, Quebec, than any man in the world, and he did not support an association. Lanza had written important texts on silicosis

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*In 1954 there was a report of peritoneal cancer in a yarn and asbestos spinner with asbestosis (Leicher 1954). The author claimed this to be the first report of this type of cancer in an asbestos worker.

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and on asbestosis and was a dominant figure in the field of occupational medicine. He did not clearly support an association. Lew was a leading health statistician, and he questioned the statistical significance of findings. W. E. Smith's review presented in Paris in 1953 seems to draw back, somewhat, from the position he took in 1952, possibly as the result of contacts with these men.

The Period 1955-63

1955

The issue of whether tuberculosis might not be a complication of asbestosis was probably kept alive by the Annual Report of the Chief Inspector of Factories. In this, Merewether analyzed 344 asbestosis deaths recorded during the period 1925-54. Of these, tuberculosis was found in 88 and cancer of the lung in 55. Merewether makes no comment on the significance of this.

A textbook by Hunter appeared which quotes Merewether's 1949 report on lung cancer in cases of asbestosis as contrasted with lung cancer in cases of silicosis. Hunter apparently believed in the interpretation of these data made by others, however, he gives no interpretation of his own.

Cartier published for the first time on the subject. His data were essentially those presented in the discussion of Smith's paper in 1952 -- six lung cancer cases among 4,000 asbestos workers between 1940 and 1950. In his 1955 paper, he also reported that these 6 cases were found in 40 autopsied cases of asbestosis, and that there were 7 cases of lung cancer in workers without asbestosis. He states that "a general survey of all employees in the industry does not seem to indicate any statistical evidence of a cause relationship." Jacob and Bohlig, writing in German, were also negative about the association. They point out that it is remarkable that cases of asbestos

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:er are found almost exclusively in the German and British literature,
the asbestos industry is by no means absent in other countries. In
4 cases of lung cancer were found among 343 cases of asbestosis.
not in excess of the incidence in the general population and they
that, "There cannot, in our opinion, be an alarming cancer expecta-
:sbestos workers." They do note, however, that for women the incidence
: than expected.

:her Smith, K. W. Smith, published a review and discussion. He
:o conflicting opinions and different reports and said these made it
: difficult to confirm or deny conclusively the relationship of
is and carcinoma of the lung. He felt the difference between the
as compared with the British and European experience was due to
use of amosite and crocidolite fibers, a harsher fiber unlike Canadian
:e os (chrysotile) used in North America. He was one of the first
:o suggest possible differences in the carcinogenic properties of
iber types.

:h reported again in a paper co-authored with Pratt-Thomas and pre-
: the 48th annual meeting of the Southern Medical Association. They
an autopsy series of 48 cases of asbestosis in which 4 lung cancers
:d. The summary states, "The possible relationship of pulmonary
a to asbestosis is as yet unsettled. Statistics would indicate a
association." In the discussion of this paper, Dr. Pratt-Thomas
d about the present industrial compensation status of lung cancer
:osis. His answer, while humorous, perhaps reflects some of the
s of that period:

"My impression is that it may not matter what opinion
e as I have testified quite volubly on one side or on
other, and the industrial commission always decides in

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the opposite direction. They would much rather listen to a doctor who has never done an autopsy, but who had 75 years of clinical experience, render an opinion they will always 'buy' rather than a so-called specialist.

Seriously, in our experience we have seen cases in which at least partial compensation has been allowed. It was thought they may not have died quite as fast if they had not gotten carcinoma and that the evidence for asbestosis producing cancer, though not proven, was sufficiently questionable so the cases were judged in favor of the plaintiff, or at least partially so."

The first case of lung cancer was reported in the Italian literature in a worker with asbestosis. This same case was reported in two separate reports (Rambola 1955 and Portigliatti 1955). This was an unusual case in which death occurred on March 30, 1954, but an autopsy was not done until June 2, 1954. After a review of the literature, both authors conclude that there is a relationship. Rombola points out that ordinarily a causal relationship is demonstrated in cancer only when the tumor can be experimentally reproduced. On the other hand, he felt that sometimes a relationship is so obvious that the requirement for experimental data should be waived — as in the case of the Schneeberg mine workers. He believed British and German literature provided adequate support for a relationship. He also thought (as did K. W. Smith) that the type of asbestos used might explain the difference between North America and other countries.

Hueper published a monograph on the environmental causes of cancer. The section on asbestos, however, is apparently a reproduction of his talk at the Seventh Saranac Symposium on Pneumoconiosis held in September of 1952 and previously cited. In an important paper, Bonser, Faulds, and Stewart (1955) reported on 12 cases of lung cancer, 2 cases of pleural cancer, and 4 cases of peritoneal cancer seen in autopsy in 72 cases of asbestosis. They point out that while no adequate comparable postmortem material from persons not exposed to asbestos is available with which to compare the incidence of lung

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cancer in asbestos workers, the incidence is very high and must be highly significant.

Hueper wrote an editorial for the American Journal of Clinical Pathology quoting from the paper by Bonser, Faulds, and Stewart and from a personal communication from O'Donnell on ten cases of asbestosis and lung cancer seen between 1940 and 1954 in a small community in Pennsylvania and occurring among employees of an asbestos textile plant. Hueper refers to epidemiologic and pathologic evidence, apparently putting weight on epidemiologic evidence. He concludes that, "Epidemiologic data available at present indicate that an increased liability to cancer of the lung is limited to the presence of asbestosis of the lung and does not extend to exposure to asbestos without the existence of pneumoconiosis resulting therefrom." In his editorial, Hueper also suggests that residence near an asbestos plant might cause bestosis and discusses the possibility of "neighborhood" cases of asbestosis and asbestosis cancer of the lung. He was the first to use the term epidemiologic in connection with studies of asbestosis and the first to suggest neighborhood contamination.

Hueper also published an experimental study. Asbestos was injected into the femur of 31 rats, the pleural cavity of 25 rats and the nasal cavity of 25 rats. He did not observe a significant number of cancers either at the site of deposition or in any remote organ. Hueper did obtain positive results in similar experiments with nickel and uranium suspensions and concluded that under proper experimental conditions the administration of chemicals in the connective tissues of rats is a reliable method for determining the carcinogenic potentialities of chemicals, such as metals, oils and dyes.

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A number of questions had been raised about the evidence showing an association between asbestosis and lung cancer. Gloyne (1951) was concerned about selective factors in autopsied material and the lack of a suitable control. Lanza (1951), Jacob and Bohlig (1955), and Bonser, Faulds, and Stewart (1955) also were concerned about a control group. Where silicosis had been used as a control, the proportion of lung cancer cases was often very low — lower than the proportion that might be expected based on mortality rates in the general population.* To some this suggested bias in autopsy material. Other concerns included the lack of experimental evidence, cited earlier, and a general confusion about the relationship of silicosis to tuberculosis and lung cancer as contrasted to the relationship of asbestosis to tuberculosis and lung cancer. Since silicosis and asbestosis were both dust induced diseases, many still felt they should present the same predisposition to other diseases.

The answer to the question about experimental evidence was not to come for several years, but in 1955 Richard Doll did provide an answer to the problem of a suitable control. In a truly landmark study, Doll carried out one of the first prospective epidemiologic investigations of an industrial population.** One hundred and thirteen men who had worked 20 years or more with asbestos were followed, and their mortality experience compared with that which would have been expected based on the experience of the whole male population. Eleven lung cancer deaths were observed against 0.8 expected. Some consider this the first epidemiologic study on the relationship between exposure to asbestosis and lung cancer, although Hueper,

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*Merewether found only 1.3% respiratory cancer in cases of silicosis. This lead to the belief that some pneumoconioses might protect against lung cancer.

**Earlier Doll (1953) had studied retired gas workers in a prospective epidemiologic study.

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apparently without knowledge of Doll's work, refers to epidemiologic studies in his 1955 editorial. Earlier reports by Merewether (1949), Gloyne (1951), and Bonser, Faulds, and Stewart (1955) qualify as retrospective epidemiologic investigations. They involved comparing the prevalence of cancer at autopsy in asbestosis cases with the prevalence in a control group — silicotics in the case of Merewether, other pneumoconioses in the case of Gloyne, and iron ore miners in the case of Bonser, Faulds, and Stewart. Results of such retrospective studies are sometimes inconclusive, however, since when positive results are obtained there is no way of knowing whether observed differences are because the study group had an unusually high proportion of lung cancer cases, or the control group had an unusually low proportion of lung cancer cases.

Doll's study was quickly brought to the attention of the scientific community. It was the subject of an editorial in the British Medical Journal (1955), and an annotation in Lancet (1955). In the latter it is stated, "Doll now confirms suggestive evidence that lung cancer is an occupational hazard of asbestos workers."

Another kind of epidemiologic study was carried out by Breslow in 1955. Starting with 518 lung cancer cases admitted to hospitals (rather than asbestosis cases as in previous studies), he selected a matched control group consisting of 518 patients admitted to the same hospitals for conditions other than cancer and other chest diseases — matched with the lung cancer patients for age, sex, and race. For each group (case and control), he inquired about their occupational histories. Among the lung cancer cases, he found 10 who had been employed 10 years or more as steamfitters, boilermakers, and asbestos workers. Among his control group he found only one such case. He refers to the earlier work by Kennaway and Kennaway (1947) and a study by Lew (1952)

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in which lung cancer was in excess in plumbers, steamfitters, and gas fitters (Lew) and in asbestos workers (Kennaway and Kennaway).

Comment on Epidemiologic Studies

Studies by Doll, Breslow, Lew, and Kennaway and Kennaway departed from other studies in that they dealt directly with the relationship between asbestos exposure and cancer, without imposing the condition of asbestosis. They answered the question, "Do workers exposed to asbestos have a higher incidence of lung cancer than workers not so exposed?" — a question suggested by Bridge and Henry (1928). Doll's study stands out, however, on two counts: first it was designed specifically to test the hypothesis of a relationship and secondly, using the general population as a control group (to determine expected deaths), he considerably reduced the bias often present in retrospective studies such as that conducted by Breslow.*

Studies by Lew and Kennaway and Kennaway also qualify as prospective studies; however, they dealt with all occupations and were not designed to test hypotheses about any specific occupation. Thus, they suffer from a multiple comparisons problem — a problem that arises when excesses are looked for in a large number of groupings of a population. Chance alone would provide statistically significant excesses in 5 out of 100 such groups ($P \leq .05$) when, in fact, no excesses exist in the parent populations.

The paper by Doll marked an end to widespread acceptance of purely clinical pathological observations regarding the carcinogenic properties of asbestosis, and opened the way for contributions by epidemiologists and biostatisticians.

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*Doll actually constructed a cohort at a point in time prior to making his observation and then examined mortality up to the then present. This method is sometimes called a historical prospective study.

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1956

Two textbooks appeared on occupational medicine which dealt with the relationship between asbestosis and carcinoma of the lung. Merewether edited a text with a chapter by Goldblatt and Goldblatt devoted to industrial carcinogenesis and toxicology. This chapter introduces the notion that asbestos is a co-carcinogen defined as "the augmentation of the action of a carcinogen by some suitable additional treatment which shows itself in increased numbers of induced tumors and/or shortening of induction time." They state further that a co-carcinogen is not in itself a carcinogen and reject the notion that the asbestos acts through purely mechanical trauma. They state that: "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." They speculate that asbestos may be soluble, but comment that it has "not given much evidence of a solubility which might be significant." By questioning the manner by which asbestos might produce tumors, the authors do not make a very strong case for asbestos as a carcinogen. Curiously, Goldblatt and Goldblatt give credit for discovery of the association between asbestosis and lung cancer to Nordmann. Also in 1956, McGee published the third edition of his "Manual of Industrial Hygiene." He quotes Behrens (1951) who, in turn, refers to the data of Merewether (1949) McGee makes no comment, but we can assume he feels these data are of some significance and that there is an association between asbestosis and cancer. He does state that pulmonary tuberculosis is less often associated with asbestosis than with silicosis.

In addition to the two books focused on occupational diseases, three books dealing with pulmonary cancer and which mention asbestosis were published. Greenblatt and Lisa discuss silica and asbestos dusts in relation to carcinoma.

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Bohlig and Jacob published a curious review. On the one hand they state that lung cancer is one of the most frequent complications of asbestosis and that predominance of lung cancer among asbestos patients in the lower lobes (3:1 vs 1:2 in the general population) constitutes the most important argument in favor of a causal association between asbestos dust and carcinoma. On the other hand, they state that statistics show that the incidence of lung carcinoma among asbestos workers is not any higher than that in the entire population. Arguments presented are similar to those in the paper by Jacob and Bohlig (1955), but it is uncertain how the authors actually feel about the relationship.

The fourth article in Italian on asbestosis and lung cancer appeared (Francia and Monarca). This consists of two reports of cancer (one lung and one pleural) in workers with asbestosis. They note that there have been only [redacted] patients with pulmonary carcinomas out of approximately 300 asbestosis cases in Italy, including the single case reported in 1955 by Rambola and Portigilotti. They contrast this with reports from England and Germany and speculate that the type of asbestos is responsible for differences between Italy and these countries (Smith 1955, Rambola 1956). They feel conclusions should be formed with caution and that experimental evidence is needed.

Uncertainty regarding the relationship between asbestos and cancer continued in North America in 1956. This is reflected in a clinico-pathological conference report on a man who worked 30 years in a Canadian asbestos mine and who was found at autopsy to have asbestosis and bronchogenic carcinoma (Todd). In discussing the case, the comment was made that, "Some claim that there is a high incidence of pulmonary lung cancer in asbestos workers. This may or may not be true."

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They state that, "The number of cancer cases reported is too small, however, to warrant causal relationship." They go on to cite the animal studies of Vorwald and Karr (1938) as not supportive of an association. In a book on pulmonary carcinoma edited by Mayer and Maier, Hammond and Machle prepared a chapter on environmental and occupational factors. With regard to asbestos, they also quote the study by Vorwald and Karr (1938) to support the conclusion that pneumoconiosis in general, and silicosis in particular, does not involve any predisposition of lung cancer. They conclude that, "Although lung cancer has been reported in autopsies of asbestotic lungs, there are at present too few cases and too little epidemiologic data to establish a significant relationship." They go on to say "... inference as to a causal relationship is not warranted." Their references include Wyers (1949), Gloyne (1951), and Wegelius (1947). These two books on lung cancer are surprising both in their conclusions, and in their limited review of the literature. The .rd book on cancer of the lung was by Weller. He concludes that, "The weight of evidence seems heavily in favor of assigning etiologic significance to asbestosis when it is found in association with pulmonary cancer." His literature review is somewhat more complete than the other two, quoting Vorwald and Karr (1938) but also Isselbacher et al (1953), Merewether (1949), Wedler (1949), Lynch (1953), and Gloyne (1951).

Hueper's ninth publication which discusses asbestosis and cancer appeared. In a paper presented in June, 1955, at a symposium at the General Meeting of the American College of Chest Physicians, he maintains his strong views about the association between asbestosis and lung cancer. He also makes the interesting observation that with one exception, all so far known exogenous respiratory carcinogens were discovered during the previous 25 years (1930-55).

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Doll's study (1955) was not referenced in a single article and reviews were otherwise far from complete. On the whole, publications in 1956 continued to be negative about an association between asbestos and cancer.

1957

If one were interested in industrial health hazards in 1957, he might have looked in the second publication by N. Irving Sax: "Dangerous Properties of Industrial Materials." He would have found that one of the dangers of asbestos dust is asbestosis, but no mention is made of pulmonary cancer. In addition to the book by Sax, two autopsy surveys, an editorial, a textbook on industrial toxicology which mentions asbestos and an animal experiment with asbestos were reported. O'Donnell and Mann reported data previously presented, in part, by Hueper as a personal communication (Hueper 1955). In their 1957 report, they reported on 13 bronchogenic carcinomas in 27 patients seen at the Lancaster General Hospital (PA) with pulmonary asbestosis. In all 13 cases the carcinoma was located in the lower lobes. They feel this lends further support "to the proposition that asbestos is a carcinogen in susceptible individuals after critical exposure in the textile phase of the industry, where asbestos dust is in high concentrations." Jones-Williams studied lungs or parts of lungs from 60 British workers with asbestosis and found 13 with associated carcinoma. His primary purpose was study of alveolar metaplasia in areas of the lung adjacent to fibrosis. In addition to asbestos workers, he studied nine other occupational groups thought to have differing incidences of lung cancer, varying from high to low. He concluded that alveolar metaplasia is unrelated to the development of pulmonary carcinoma.

Lancet published a leading article on industrial lung cancer. Six industries are listed in which "... the hazard of lung cancer is well

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established." Among these is the asbestos textile industry. They state hat, "In this form of industrial cancer; there is no doubt that fibrosis precedes the malignant process, and it is clear that the exposed female is susceptible to the disease."

The second edition of Fairhall's "Industrial Toxicology" appeared. Asbestos is discussed and reference is made to Doll's conclusion that lung cancer is a special hazard of asbestos workers. Curiously, however, cancer is not listed among the complications or sequelae of pulmonary asbestos: purulent bronchitis, bronchial pneumonia, pulmonary tuberculosis and emphysema.

Lynch, McIver and Cain reported on an animal experiment involving 127 mice dusted with asbestos and 222 control mice. Single and multiple tumors were observed in each group; however, none were malignant and the authors were "... unable to demonstrate any proof of the carcinogenicity of asbestos under the conditions of this experiment ..." They felt their results were equivocal and that future experiments should use larger animals. In their comments they point out that in the literature there are "no very large groups of cases ..." and "... one is beset with the problem of deciding whether the cases reported are weighted in favor of a high incidence of carcinoma by selection." In general the tone of their article is negative with regard to an association. Doll's work is not cited. Credit for reporting the first carcinoma of the lung associated with asbestos is given to Lynch and Smith. The work by Nordmann and Sorge (1941) is discussed with the comments that the number of animals (10) is very small, no suitable control animals are mentioned and that in a personal communication from L. U. Gardner he regarded their observations as "merely suggestive."

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1958

Another animal experiment (Schmahl) was reported — this time in German — involving subcutaneous and intraperitoneal implantation of asbestos in rats. Of a total 39 rats, 30 survived longer than 15 months and of these, 15 developed sarcomas at the site of implantation. The author considers this "renewed evidence that a substance which causes cancer in man will provoke the same effect in animal experimentation." They consider Nordmann and Sorge's 1941 report as the first experimental work supporting an association.

Bohlig and Jacob published again (German) making some of the same points they made in their 1956 article. They counted 18 cases of asbestos lung cancer reported in Germany between the years 1938 and 1956, and 80 cases in the world literature prior to 1956. They attribute most of the total to English autopsies and feel these cannot be used to generalize since autopsy material was not selected at random. They conclude that the incidence of asbestos lung cancer among males is not higher than lung cancer in the general population, but that females do have a higher incidence. One would conclude from this paper that Bohlig and Jacob are skeptical of an association particularly in males, although, as in their earlier work (1956), they sometimes write as though they believed an association truly existed.

An epidemiological investigation was reported by Bruan and Truan. This was an important study for three reasons. It was the first prospective epidemiological study conducted in North America, and the second ever conducted (Doll, 1955, was the first). Second, it was the first study of asbestos miners ever undertaken. Finally, it included a critical review

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of the world literature with 92 references.* In their review, the authors generally criticized reports based on autopsy material as highly selective and point to the probability of duplications in cases put together for review articles. They also describe advantages of the epidemiologic method, noting that in order to draw generalizations about all asbestos workers, it is necessary for a study to include living as well as dead persons. The problem for their study was to determine whether asbestos miners experienced more lung cancer than did the general population (a problem like that formulated by Bohlig and Jacob, and by Doll). They developed a cohort of 6,091 men who worked five years or more in the asbestos mining industry in Quebec, Canada, and were in the industry in 1950. As of 1955, they reported that the rate of "proved" cases of lung cancer (25.3 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." They conclude that asbestos miners do not have more lung cancer than the general population. Moreover, lung cancer among the miners "does not appear to increase with length of exposure or degree of exposure, a fact which presents strong evidence against the carcinogenicity of asbestos."

Goldblatt, who wrote the section on asbestosis in Merewether's book (1956) published a review on occupational carcinogenesis. He cites Merewether's 1949 report and Doll's 1955 report as confirmation of asbestosis and lung cancer, and reviews Doll's paper in considerable detail. He also points to the lack of experimental evidence and reiterates his views on asbestos as a co-carcinogen and outlined in Merewether's book. A paper in French by Chauvet appeared in 1958 reporting on an autopsy in a worker

*Only 26 of these are actually referred to in the paper. The reason for the remaining references is unclear.

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who prepared circular joints from asbestos. Both asbestosis and lung cancer were present and the author believed this illustrates a causal association.

1959

Prior to 1959, Bohlig, who along with co-authors had published papers in 1955, 1956, and 1958 on the relationship between asbestosis and lung cancer, seemed generally uncertain about the relationship. Their argument was essentially the same as that proposed by Braun and Truan (1958). That is, if asbestos causes lung cancer, then workers exposed to asbestos should have more lung cancer than workers not so exposed. This is a purely epidemiological argument, and, in fact, is one of the conditions for proof of a causal relationship proposed by Bridge and Henry (1928). Hueper (1955) rejected this notion: "It is quite immaterial how many workers employed in the industry develop lung cancer, since an undetermined portion of these workers undoubtedly sustains either no exposure or only a low intensity exposure and does not develop asbestosis of the lung, which is the prerequisite for the subsequent cancerous development." In 1959, Bohlig, writing with Jacob and Kallobis, seemed to join Hueper in his general views about the meaning of an excess or lack of excess in lung cancer among asbestos workers — but with a different logic. These authors now argue (Bohlig, Jacob, and Kallobis) that, despite their inability to demonstrate an excess in male asbestos workers, the causal association is evidenced by the fact that asbestos lung cancers are located in the lower lobes of the lung and female asbestos workers have a relatively high rate of asbestos lung cancer. They conclude that the removal of asbestos lung cancer from the list of occupational injuries would therefore not be justified.

The views of Bohlig and Jacob (expressed prior to 1959) and of Braun and Truan (1958) were criticized in the German literature by Bohme. Bohme wrote two articles. The first reported 6 lung cancer cases in asbestosis

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cases at autopsy, and the second reviewed insurance records of 125 asbestos workers with compensable disease and found 15 recognized cases of lung cancer. Of the 125, 31 had died of which 11 had lung cancer confirmed by autopsy or biopsy. Bohme pointed out that lung cancer is thus the most frequent cause of death among asbestotics. He felt that the conclusion of Bohlig and his co-authors, and of Braun and Truan are "invalid," apparently for the reasons stated by Hueper — in effect, because when whole populations are studied findings are diluted by workers with little or no exposure. If one confines observations to workers who have sufficient exposure to asbestos to develop asbestosis, then the true facts emerge.

DuBois and Geiling published a "Textbook on Toxicology." In a section on asbestos, they stated, "Only recently has asbestos been recognized as a cause of lung cancer in workers exposed to the dust of this material." They go on to state that 92 autopsies on patients showed 14 had lung cancer, and that an animal experiment was conducted in which 20 percent of the animals developed squamous cell carcinoma. The authors of these studies are not identified; however, the second is probably the work of Nordmann (1938). Homberger edited a book on the "Physiopathology of Cancer" in which Hueper prepared a chapter on environmental cancer. Hueper's views are as in previous papers: "Carcinogenicity of asbestosis is by now definitely established ..." He cited 110 cases of lung cancer co-existing with asbestosis from the United States, England, and Germany. He also stated, "The experimental reproduction of lung cancer in mice has been reported," but gives no reference. He must be referring to Nordmann and Sorge's work (1938) since Schmahl (1958) who felt he had the only other positive study worked with rats. This is interesting in view of Hueper's apparent reservations of Nordmann's work (Hueper 1955).

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Eckard published a book on "Industrial Carcinogens." He clearly believed there is a relationship between asbestosis and lung cancer and quoted extensively from the Annual Report of the Chief Inspector of Factories for the year 1954. Pointing to a lower mean age at death of persons with asbestosis alone as compared with persons with asbestosis and lung cancer, he concluded that asbestosis, uncomplicated by lung cancer, posed a greater threat to longevity than when lung cancer is present. He went on to conclude that the control of asbestosis should eliminate "this occupational cancer." Eckart also raised the question as to whether the etiologic agent may not be some mineral impurities in asbestos, rather than asbestos per se. He pointed to the study of Braun and Truan (1958), which he felt suggested that the causative agent of asbestosis may be different than for lung cancer since there was asbestosis among the Canadian miners studied but, according to Braun and Truan, no lung cancer hazard.

A general medical textbook appeared edited by Cecil and Loeb. A chapter by Christie on pneumoconiosis lists carcinoma of the lung as having a high incidence in cases of asbestosis — "as high as 13 percent." Writing in French, Nordvik studied the problem of silicosis and asbestosis as they relate to pulmonary cancer and presented a case where silicosis and cancer co-existed. He concluded that the question of silicosis and cancer remains controversial, while he felt arguments for a relationship between asbestosis and cancer are more convincing. He accepted "temporarily at least" the latter relationship.

1960

Three textbooks in occupational medicine appeared in this year. Zeltnstone and Miller published with a chapter dealing with occupational

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cancer. They consider three categories of carcinogenic materials: established, suspected but in dispute or unproven, and established for animals only. They place asbestos in the suspected category. They comment, "In the United States, particularly since the studies of Braun and Truan, there is considerable conviction that asbestosis does not predispose to the development of lung cancer. Until further evidence is forthcoming, we have arbitrarily placed asbestos in the unproven or doubtful group." Fleming, D'Alonza, and Zapp published with a chapter on occupational chest diseases prepared by G. W. H. Schepers. His comment was that, "Pulmonary carcinoma has been observed with such a high frequency in employees of the asbestos industry that a causal relationship has been accepted by most authorities. Indeed, pulmonary carcinoma is compensable as an occupational disease in England, Germany, and South Africa." Schepers also noted that pleural mesothelioma is also prevalent, especially in the crocidolite industries. No references were given. Schilling published with a chapter on Industrial Pulmonary Diseases prepared by J. C. Gilson. On the subject of asbestos and lung cancer, Gilson refers only to studies by Doll (1955) and Braun and Truan (1958). He apparently feels both are correct and the difference in results is related to the type of asbestos to which the men in these studies were exposed. In support of this, he refers to observations by Sleggs and Wagner (1960) on mesothelioma discussed below.* He also quotes a personal communication from Knox which suggests that among men exposed only after the introduction of dust control measures in 1931 (the Asbestos Industry

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*Gilson must have seen a prepublication copy of the 1960 paper by Wagner, Sleggs, and Marchand.

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Regulations) the lung cancer rate is no different than that in the general population.

Dunn, Linden, and Breslow reported on a prospective epidemiological study of asbestos workers, the second to be carried out in North America, the third in the world literature. Several occupational groups were studied in addition to asbestos workers. 7,836 asbestos workers were identified and followed for the years 1954-58. Nineteen cases of cancer were observed where 13.7 would have been expected based on the estimated rates for the general population of the State of California. After adjustment for cigarette smoking and other factors, observed and expected deaths for lung cancer were 22 and 15.6. Under these conditions, the excess in lung cancer for asbestos workers was not considered significant. Two other occupations, cooks and painters were identified as having a significant excess. The authors are cautious in their conclusions, however, and consider this only a preliminary report. While not specifically stated, the asbestos workers studied were apparently asbestos insulators.

Anderson and Campagna reported a case of asbestosis with carcinoma of the lung and a literature review in which they were able to identify 24 other such cases.* They ask for more frequent reporting of asbestosis cases with and without neoplasia, with careful attention to smoking and feel only when these facts are available will final assessment of the relationship between asbestosis and lung carcinoma be possible.

Konig reported on an autopsy survey of 36 cases of asbestosis and noted seven cases of lung cancer, four cases of pleural cancer, three cases of peritoneal cancer, and four cases of stomach cancer. He commented on the apparent inconsistency in papers by Bohlig and Jacob (1955, 1958) stating [illegible] counted 110 such cases by 1959.

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that they conclude that lung cancer is no more frequent in asbestos workers than in the general population, and yet they consider the causal relationship between pulmonary asbestosis and bronchial carcinoma a proven fact. Konig felt the peritoneal cancers were particularly significant and referred to an earlier paper by Leicher (1954) on these cancers. He also felt stomach cancer was in excess.

Keal reviewed the literature quoting data by Merewether (1949), Wyers (1950), Gloyne (1951), and Doll (1955) as supporting an association with lung cancer and Jacob and Bohlig (1955) and Braun and Truan (1958) as not accepting an association. He reported on 42 cases of asbestosis from hospital records among which there were 30 deaths. Among the deaths there were 14 who died with lung cancer. He also drew attention to a bronchial carcinoma in one patient without asbestosis, but whose sputum contained asbestos bodies many years after removal from exposure to asbestos. Also, in Keal's series 9 of 15 women who died with asbestosis also had ovarian or peritoneal cancer. Only one out of 15 men dying with asbestosis had peritoneal cancer.

A very influential study on pleural mesothelioma was published by Wagner, Sleggs, and Marchand. Prior to 1960, pleural cancers had been noted by Gloyne (1933), Wood and Gloyne (1934), Wedler (1943), Behrens (1951), Cartier (1952), Weiss (1953), Leicher (1954), Bonser, Faulds, and Stewart (1955), Doll (1955), Bohlig and Jacob (1956) and Van der Schoot (1958). Only three of these writers had definitely associated pleural cancers with asbestos (Wedler, Weiss, and Leicher). All three of these, interestingly, published in German.

The paper by Wagner, Sleggs, and Marchand was of importance not only because it focused on primary malignant tumors of the pleura in relation

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to asbestos, but also because of the emphasis they placed on the probable special carcinogenic properties of crocidolite asbestos. Other writers (e.g.: Smith 1955, Gilson 1960) had speculated on possible differences in the carcinogenic properties of various types of asbestos, but Wagner et al presented epidemiologic evidence for such a difference. They reported 33 cases of primary malignant tumors of the pleura. All but one had probable exposure to crocidolite asbestos (Cape Blue). This is a rare tumor and there was, in fact, some question at that time as to whether such tumors actually existed. The paper by Wagner et al greatly extended the field for research on the biological effects of asbestos and set the stage for much of the research effort that was to follow.

1961

An interesting exchange took place in the Questions and Answers section of the Journal of the American Medical Association. A physician from Georgia asked whether there was any evidence that silicosis will or can produce cancer of the lung. R. T. Johnstone replied that there is no epidemiologic evidence that free silica produces lung cancer. He added, however, that of the several silicates, asbestos is under suspicion, especially in Great Britain. He then stated, "In the American literature there is no evidence that there is a relationship between asbestosis and lung cancer." George M. Trimble replied, disagreeing with Johnstone with regard to asbestos, and quoting Stoll (1951), Isselbacher et al (1953) and E. Cuyler Hammond (Mayer and Maier 1956) who felt the evidence was "suggestive." Johnstone replied quoting Paul (JAMA 175:601, 1961) on the importance of epidemiological evidence, stating that "there is no epidemiological evidence among American workers, and quoting Hinshaw and Garland (1956) who state, "The [illegible] has not been fully confirmed." Johnstone placed much weight on

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epidemiologic evidence. He was right in that neither of the American prospective epidemiologic studies (Braun and Truan 1958, Dunn, Linden, and Breslow 1960) had been interpreted as supporting the hypothesis. Actually, the statistician-epidemiologist, E. Cuyler Hammond, did not lend strong support to the relationship.

Sleggs, Marchand, and Wagner published again on pleural cancers; this time adding one case. Of a total 34 cases, 33 gave a history of exposure to crocidolite asbestos mined in the North West Cape of South Africa. J. F. Knox, in a letter to the editor of Lancet, disagreed with the conclusions of Keal (1960) with regard to a relationship between abdominal cancer and asbestos. He reported no ovarian or peritoneal cancers in 30 women with asbestosis. Frenkel and de Jager reported (in Dutch) a pleural mesothelioma in an asbestos insulator and concluded that the connection between the patient's asbestos dust exposure and the mesothelioma was very probable. Heard and Williams reported on three lung cancers and one case of peritoneal mesothelioma in six cases of asbestosis. They felt there is little doubt there is an increased frequency of lung cancer in asbestosis and, moreover, that these effects may not be confined to the lungs. They noted, however, that all their cases were heavy smokers.

Telischi and Rubenstone reported a bronchogenic squamous-cell carcinoma, a bronchial adenoma, and an adenocarcinoma of the stomach seen at autopsy in a "plaster mixer" with asbestosis. They accepted the relationship between the lung cancer and asbestosis, but did not consider likely any relationship between gastric carcinoma and pulmonary asbestosis. A review and discussion of asbestosis research was published in Polish (Szczikiewicz). Regarding asbestosis and lung cancer, the conclusion was that lung cancer is enhanced to a greater extent by asbestosis than by

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s[illegible]cosis. This review placed Merewether (1949), Wedler (1943), Gloyne (1951) and Doll (1955) as favoring an association, and Rambola (1955), Braun and Truan (1958), and Cartier (1955) as being against an association. Another Polish article (Krzymein and Wolska) accepted the association based on the American textbooks by Homberger (1959) and Cecil and Loeb (1959).*

1962

Three papers devoted solely to asbestos and mesothelioma appeared. McNutly reported from Australia on a pleural cancer in an asbestos mill worker exposed to crocidolite asbestos and felt this confirmed the work of Wagner et al (1960). He felt that this type of asbestos is a "very harmful and lethal fibre." Thompson reported on seven cases of mesothelioma, four pleural and three peritoneal. None had asbestosis clinically. Six of these had a[illegible]stosis microscopically, however, all had either worked with asbestos or lived in areas where it was mined. Thompson was concerned about the enormous increase in the world consumption of asbestos and the possibility of a marked increase of mesothelioma in people who have occupations in which exposure is too slight to cause clinical asbestosis. Smither, Gilson, and Wagner, in a letter to the editor of the British Medical Journal, expressed concern over lack of correlation between the severity of pulmonary asbestosis and the occurrence of mesotheliomas. They felt more information was needed on exposure for such cases and asked for information concerning any patient in whom this type of tumor had been diagnosed. A method for differentiating between pleural mesotheliomas and peripheral pulmonary adenocarcinomata was noted. McCaughey, Wade and Elmes replied, reporting asbestos bodies in 12 out of 15 cases of diffuse pleural mesothelioma. In only one, however, were asbestos

*[illegible] no opinion on the subject but note the high incidence [illegible] patients with asbestosis.

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dies plentiful. In four out of nine who died since 1950 there was a clear-cut history of exposure. In most cases exposure was not continuous or prolonged, however. A reply was also received from Enticknap who was not in favor of the term mesothelioma since he felt the existence of this neoplasm was by no means universally accepted. He preferred the term "the peritoneal tumor of asbestosis."

Hunter published the third edition of his book, "Diseases of Occupations." In it he cites post-mortem data published in the 1949 Annual Report of the Chief Inspector of Factories (Merewether 1949), Doll's study, the 1958 findings of Braun and Truan, which he referred to as "a careful epidemiological survey," Keal's 1960 findings, particularly in regard to peritoneal cancer, and the 1960 report by Wagner, Sleggs and Marchand. He did not comment, however, on his interpretation of conflicting reports but gives the impression he believes in the association.

In 1962 Wagner published the first paper on experimental induction of mesothelial tumors of the pleura in rats, and what might be the first widely accepted experimental evidence on the carcinogenicity of asbestos fibers (depending on how one views Nordmann's 1938 findings and the sarcomas produced in the 1958 experiment by Schmahl). Of 30 rats with crocidolite asbestos injected in the pleural cavity, two developed mesothelioma; of 20 rats injected with chrysotile, one developed a mesothelioma; and of 10 injected with silica, one developed a mesothelioma. His only comment was that the production of tumors by chrysotile and silica complicated the interpretation of his findings.

Several reports on asbestosis and cancer of the lung appeared. Cordova, [illegible] and Knudtson reported on eleven lung cancers in eleven cases of asbestosis (at autopsy or surgery). They cited Bridge and Henry's 1928 paper

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outlining conditions for the acceptance of industrially acquired cancer and acknowledge that these conditions had not as yet been fulfilled for asbestos. Nevertheless, they concluded that there is sufficient clinical pathological evidence to make it highly probable that asbestos is a carcinogenic agent. Fingerland and Jindrichova published the first paper in Czechoslavakia on the subject and reported on one case of lung cancer at autopsy in a man with asbestosis who had worked 22 years in a workshop with a high asbestos dust concentration. They felt this is a causal relationship quoting Nordmann (1938), Gloyne (1951), and Merewether (1949). They add that in their case possibly past tuberculosis and cigarette smoking were also involved.

Three papers appeared in French. Champeix, DeLaguillaumie, Jacquemet, and Geille reported on a single case of asbestosis and lung cancer. The lung cancer proved at autopsy to not be primary, and they felt their observation showed the difficulty of diagnosing primary bronchial cancer. They concluded that utmost care must be taken before linking this type of cancer with occupation. Another paper by DeLaguillaumie, Champiex, and Jacquemet, reported on the same case and considered the association between asbestosis and lung cancer probable based on their review of the literature. They pointed out that in France the notion of an association was a new one. Dandrigal, Tabbara, Proteau, and Derobert reported on a case of co-existing asbestosis, tuberculosis and lung cancer. They quoted Delarue and Paillas who reject the carcinogenic role of chromium and asbestos.* Their conclusion was that there is no connection in their case between the lung cancer and the asbestosis.

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*Societe Anatomique de Paris, April 13, 1961.

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The Period 1963-64

1963

The third North American prospective epidemiological study appeared. Mancuso and Coulter identified 1,495 employees of an asbestos products plant who were working sometime in 1938 or 1939. They followed these workers from 1940 to mid-1960 and observed 15 lung cancer deaths among males vs 5.4 expected, and four among females vs .19 expected. They also observed three peritoneal cancers vs .08 expected. In addition, review of histological material for cancer deaths identified two peritoneal mesotheliomas. This paper was directed at developing a method for using U. S. Social Security records for identifying and following industrial cohorts. It contains no literature review to support an argument for a relationship between asbestos lung and peritoneal cancer. However, it is clear the authors believed this relationship existed. They felt that asbestos initiated histologic change sufficient to initiate the carcinogenic process, although it may not reach the stage of clinical or X-ray evidence of asbestosis. The plant studied by Mancuso and Coulter is the same plant studied earlier by O'Donnell and Mann (1957). The title and focus of Mancuso and Coulter's paper may have prevented frequent referencing in literature dealing with asbestos and cancer. It was the first positive American prospective epidemiological investigation on the subject.

Two reviews of lung and pleural cancer in relation to asbestos were published. Walters acknowledged the problem of pulmonary malignancies and asbestos in South Africa. Leatheart and Sanderson published some observations on trends in asbestosis in Great Britain and noted that despite the regulation of dust in the asbestos industry since 1933, asbestosis was still occurring. Nearly half of the certified cases in the preceding two years occurred in insulators, whose work was not covered by the regulations. They felt that

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efforts should be made to find a substitute for asbestos. They also noted that in a minority of asbestosis patients, a fatal lung cancer develops, and "we seem to have been seeing this termination more frequently in recent years." In a discussion of this, Smithers pointed out that there is evidence of the effectiveness of dust control measures as evidenced by a decline in new cases in the late forties and early fifties and an increase in years of exposure before diagnosis of asbestosis. Dr. Smithers added that he believed type of asbestos is important in malignant mesothelioma.

In the "Case Records of the Massachusetts General Hospital," edited by Castleman, L. H. Knowles briefly reviewed the history of asbestosis, quoting from Hunter (1957). He stated that, "There seems to be general agreement at the present time that bronchogenic carcinoma is associated with asbestosis. The evidence is inferential but persuasive." He quoted Telischi and Rubenstone (1961), Wagner, Sleggs, and Marchand (1960), and Isselbacher and his associates (1953). The case under discussion was a 56-year old plumber. The diagnosis was asbestosis and pleural mesothelioma.

In reply to the 1962 appeal in the correspondence section of the British Medical Journal by Smither, Gilson, and Wagner for information on patients with malignant mesothelioma, J. G. Thompson wrote from South Africa pointing out that he recently described a new pulmonary condition, basal asbestosis, which is associated not only with mesothelioma of the pleura but also of the peritoneum. This condition produced no pulmonary signs or symptoms and is not evident clinically, and since it does not shorten the patient's life it produced more malignant tumors than asbestosis. Thompson also published an article which attracted much attention and set the stage for a new area of investigation. He reported that in 500 consecutive autopsies on subjects 15 years of age and over, 132 or 25.4% showed asbestos bodies,

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only 6% of which were thought to be occupational in origin. He felt this clearly demonstrated that asbestos was being inhaled by urban dwellers and that more cases of basal asbestosis would seem most inevitable. He felt that if he is correct about basal asbestosis an increase in mesothelioma will follow."

In reply to Thompson's letter to the British Medical Journal, J. P. Lawson wrote that he had observed calcified pleural plaques overlying the diaphragm in two patients with acute abdominal discomfort. Both worked with asbestos, and he postulated that abdominal discomfort might have been due to peritoneal involvement by asbestos fibres and may be another presentation of asbestosis. Subsequently, Lawson wrote to report that one of the patients died and post-mortem examination showed asbestosis and involvement of the peritoneum by tumor tissue.

A case report appeared in Italian on an insulator with asbestosis and lung cancer. Farina and Mazzanti reported this single case and felt it was relatively rare since they had seen 30 other cases of asbestosis without cancer. They felt that asbestos alone has only a predisposing action to cancer.

Lanza published a textbook on the pneumoconioses. The chapter on asbestosis was prepared by K. W. Smith. Smith took a largely negative view on the relationship between asbestos and lung cancer. He criticized reports which associated lung cancer and other conditions with asbestos workers. He stated that, "Perhaps with more accurate reporting, the alleged association of inhalation of asbestos fibre with other intercurrent disease conditions would be clearer today. It is entirely possible that the asbestos fibre may be a carcinogen, or a co-carcinogen. However, the true relationship will remain obscure until responsible reporters can evaluate the relationship

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between agent and disease and not just job title and disease." He went on to state that in over 50,000 physical examinations among workers in asbestos mining, milling, and fabricating operation where exposure was only to chrysotile fibers, there were no more cases of pulmonary malignancy than among the general population.

1964

Another type of epidemiological study was published. Oettle studied the geographic distribution of cancer of various sites and histopathologic types in Africa. He felt data suggested that more than 80 percent of cancers affecting Western races are environmentally induced and potentially preventable.* He found a three-fold excess in lung cancer mortality in the areas of South Africa containing asbestos mining operations when compared with areas without asbestos mining but with similar populations and a similar degree of urbanization. Areas adjacent to asbestos mining districts had intermediate lung cancer mortality rates. No significant differences or comparable trends were noted for cancer of the esophagus, stomach, ovary or bladder.

In addition to Oettle's epidemiologic observations, two historical prospective epidemiological investigations of asbestos exposed populations were reported. This brought the number of this type of study in the world literature from three (Doll, Braun and Truan, and Mancuso and Coulter) to five. Elwood and Cochrane studied 1,153 men and 269 women who worked six months or more after 1936 in an asbestos works (sheeting for building and pipe lagging) and were exposed only to chrysotile asbestos. The study was planned primarily to see if pleural mesothelioma was a common cause of death

* It is a currently popular quotation not, however, attributed to Oettle.

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in workers exposed primarily to chrysotile asbestos dust. The authors concluded that, "No evidence has been obtained to suggest that in the group studied this was the case as only one man ... had died from this cause." Of workers with 15 years or more since first exposure, seven cases of respiratory cancer were observed, however, as compared with 3.02 expected. The authors felt this finding was "in accordance with results of other studies in this field." The low risk of death from pleural mesothelioma suggested to the authors that chrysotile asbestos may not be an etiologic factor in pleural mesothelioma.

Selikoff, Churg, and Hammond studied 632 insulation workers with a minimum of 20 years since first exposure to asbestos. They observed 43 respiratory cancer deaths as compared with 6.6 deaths expected. There were three pleural mesotheliomas and one peritoneal mesothelioma. They also observed cancer of the stomach, colon, and rectum in 29 cases compared to 9.4 expected. They concluded that "the results are clear, and exposure to asbestos results in a marked increase in the incidence of cancer of the lung." They also noted that the incidence of mesothelioma death was "strikingly high." This was the first U. S. study to show such a high incidence of asbestos-related cancer. Doll, in England, added to his 1955 observations in a general paper on susceptibility to cancer. Of 104 men employed more than years in an asbestos products plant, 20 lung cancer deaths were observed areas less than 2 were expected based on national mortality rates.

A number of papers on malignant mesothelioma were published in Great Britain in 1964. Owen reported 16 cases of pleural mesothelioma and case of peritoneal mesothelioma over a period of eight years from the pool (England) area. Strong evidence of exposure to asbestos was in 14 of the 17 cases. He concluded that exposure to asbestos is

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a major factor in the causation of diffuse mesothelioma. Hourihane reviewed 34 cases of confirmed mesothelioma from London (England) and of 30 where lung parts were available, he found asbestos bodies in 15. He pointed out that the majority of his cases did not have asbestosis before death and many gave no history of industrial exposure. Fowler, Sloper, and Warner reported on three pleural mesotheliomas, also from the London area, two without clinical signs of asbestosis. All had asbestos bodies present at autopsy. They felt the association between asbestos and mesothelioma is unlikely to be fortuitous. Enticknap and Smither reported 11 cases of abdominal tumors in association with exposure to asbestos from Essex (England). They felt a remarkable feature of these cases was the minimal fibrosis found in the lungs. No patient was completely disabled by pulmonary fibrosis.

There continued to be reports of lung cancer associated with asbestosis. Navratil reported five cases of lung cancer in 39 cases of asbestosis. He felt the frequency of lung cancer in asbestosis was high compared with the male population of the Central Bohemian region (Czechoslavokia). His major interest was the association between asbestosis and tuberculosis, a problem he concluded needed investigation by international cooperation. Noenincks (French) reported three cases of lung cancer — one with, in addition, a malignant peritoneal tumor out of 10 patients he had treated with asbestosis. He felt under certain conditions disease produced by inhalation of asbestos can lead to the development of malignant disease. Buchanan updated the annual reports of the British Chief Inspector of Factories (Merewether 1949, 1954, 1955) in regard to lung cancer among cases of asbestosis. He noted that since asbestosis is a compensatable industrial disease in Great Britain, a high proportion of cases are recognized during life, and in the event of death, there is an autopsy examination. During the period 1931-62, a total of 364 males were seen with asbestosis, and

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lung cancer was present in 99 or 27.7%. This proportion increased steadily from 18.2% for the period 1931-40 to 44.9% for the period 1961-62. For females comparable percentages were 11.9% overall; 6.1% for the period 1931-40 and 18.2% for 1961-62. He also noted nine pleural mesotheliomas of which four were seen in the period 1961-62. He felt "it is beyond question that there is a considerably greater risk of dying from lung cancer or mesothelioma if asbestosis is present." In America, Gafafer published a book on occupational diseases. With regard to lung cancer and asbestosis he states:

> "The conflicting opinions and differences in reports make it difficult to confirm or deny conclusively a causal relationship between asbestos and cancer of the lung or extrapulmonary tissue. However, there is increasing evidence to suggest that such a relationship exists."

Several reviews appeared on the subject of asbestos and cancer. Murray discussed pleural cancer in relation to type of asbestos in Africa. He acknowledged that while all evidence pointed to crocidolite asbestos, this type of asbestos had been mined since the turn of the century while chrysotile and amosite had only been mined since World War II. He felt more time is needed to see any effects of these two types of asbestos.

The Committee on the Nature and Prevalence of Asbestosis of the American College of Chest Physicians issued a report. Regarding lung cancer and asbestosis, they stated that there are more articles favoring a positive relationship than denying a relationship:

> "While it has been reported that there may be an enhanced prevalence of pulmonary neoplasia in some asbestos industries (e.g. crocidolite or amosite) as in some locations (e.g. South Africa, England), this does not appear to apply to the chrysotile industry in North America. This comment applies both with respect to intrapulmonary new growths and to pleural mesothelioma."

Kogan, in a Russian review of lung and pleural cancer in relation to asbestosis, noted the higher percentage of lung cancer seen by most authors

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among asbestotics, but also cites Bohlig, Jacob, and Kallobis (1959), Braun and Truan (1958) and Cartier (1955) that lung cancer is no higher in asbestos workers than in the general public. He stated that a number of authors consider — not without reason — that data obtained from autopsy findings are inadequate proof and notes that so far, in the Soviet literature, this problem has not been studied. This article is interesting in that it is a kind of fourth party reaction to the British-German-American literature of that period.

One animal study appeared. Smith, Miller, Churg, and Selikoff reported one case of pleural mesothelioma in 45 hamsters injected with amosite asbestos. Twenty-nine survivors were still being followed at the time of their report.

The 1964 Conference

Thirty years after Gloyne's first paper on asbestosis and lung cancer a conference was held by the New York Academy of Sciences on the Biological Effects of Asbestos. One session was devoted to experimental studies of asbestos and neoplasia, one to epidemiological studies of neoplasia, and one to diffuse mesothelial tumors. Of a total of 65 papers presented, 23 dealt to varying degrees with asbestos and cancer. On the question as to whether asbestos caused cancer, no opinion was expressed in three papers, while 20 supported a relationship. On the question of whether asbestos caused mesothelioma, no opinion was expressed in four, while the remaining 19 supported a relationship. There was a considerable difference of opinion on the question as to whether it was necessary for pathologically detectable asbestosis to be present for a causal relationship between asbestos and lung cancer. As J. C. Wagner put it:

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> "On current evidence, the earlier view that carcinoma of the lung occurs in cases with a significant degree of asbestosis is strongly supported, but information is still required to confirm that there is no correlation between exposures per se and these tumors (i.e. in the absence of asbestosis)."

J. C. Gilson, in a discussion of unresolved problems associated with human exposures to asbestos also reflects this view. In addition, he saw as unresolved problems in regard to cancer: (a) the relationship of the type of asbestos to asbestosis, bronchial carcinoma, and mesothelial tumors and (b) the need for systematic prospective [epidemiological] studies of workers in asbestos.

There can be no doubt that the question of whether asbestos caused carcinoma of the lung and diffuse mesothelioma of the pleura and peritoneum was settled at the 1964 conference. Probably the best indication of the views expressed at the conference and of the questions that remained to be answered is contained in the report of a Working Group on Asbestos and Cancer sponsored by the International Union Against Cancer. This working group met at the time of the conference, under the chairmanship of Thomas Mancuso, and their report was published in August, 1965.

In 1964, the Johns-Manville Corporation placed the following warning label on packages containing its asbestos products:

> "This product contains asbestos fiber. Inhalation of asbestos in excessive quantities over long periods of time may be harmful. If dust is created when this product is handled, avoid breathing the dust. If adequate ventilation control is not possible, wear respirators approved by the U. S. Bureau of Mines for pneumoconiosis-producing dusts."

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CONTEMPORARY OPINIONS

While some of the writers directly indicate how they feel about the relationship between asbestos and cancer, many do not. In most cases careful reading of their papers does, however, make it possible to form an opinion as to their attitudes. In the preceeding review of the literature, excluding the proceedings of the 1964 New York meetings, a total of 94 writings were referenced on the subject of asbestos (or asbestosis) and cancer. In addition, there were 10 papers published in 1965 which were not reviewed, but which will be dealt with in this section.

Asbestos and Lung Cancer

As a method of summarizing how at different points in time, the writers were interpreting the literature and observations then available on the subject of asbestos (or asbestosis) and lung cancer, I classified the impression about the relationship between asbestos and lung cancer I gained from reading each of the 104 articles as: (1) asbestos definitely causes lung cancer, (2) asbestos possibly causes lung cancer, and (3) the relationship is unproven or asbestos does not cause lung cancer. For the first two categories, a subdivision was made as to whether I felt the writer thought asbestosis must or must not be present.* Entirely independently, I.T.T. Higgins kindly classified the same articles in the same manner, using the same material.** Where disagreements occurred between Higgins and myself, they were discussed and resolved. The end product appears in Table A. This table also indicates the type of article, whether the original article was in some

*One of my student assistants (N.S.) checked and often improved my classification.

**Dr. Higgins is a Professor of Epidemiology, School of Public Health, University of Michigan.

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language other than English, and whether the author conditioned this opinion on type of asbestos fiber. In a few cases involving negative animal experiments, the paper has been put under the unproven column even though the writer may have personally believed in an association between asbestos and cancer (eg: Hueper 1955). Generally, however, where original data were presented, the writer's opinion coincides with what the data seem to show. Table A provides sufficient information to locate any single writing in the bibliography. Where textbooks had chapters written by other than the author or editor, the name of that writer appears in parenthesis after the name of the textbook author or editor.

Data in Table A clearly parallels the narrative in the preceding section. A shift in opinion can be seen with the passage of time up to the year 1942. The retreat from a definite decision in 1956 can clearly be seen, and there appears to be not much movement toward the "definitely" column until 1965. The decade 1956-1965 seemed to be one of uncertainty with little change in the position of individual writers. In fact, with the exception of Bohlig, individual writers rarely changed their position on the subject.

Nordmann was the first to make up his mind, followed closely by other German writers. The American, Hueper, was not far behind. Gloyne and Lynch never moved to the "definitely" column, while even as late as 1965 there is an entry in the unproven column. Textbook writers were among the last to acknowledge a relationship, whereas writers of editorials were among the first. Note, for example, that after 1951 there are no editorials in the unproven column but five textbooks.

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Starting in 1955 there was a shift to the notion that asbestos can cause lung cancer without asbestosis, although this issue was somewhat clouded with the introduction of the idea of microscopic asbestosis — that is, asbestosis that causes no clinical signs or symptoms but which was seen at autopsy. English language articles were clearly in the majority after WWII.

Asbestos and Mesothelioma

Rare diseases, like malignant mesothelioma, are relatively easy to identify with occupational exposure and many of the problems in linking lung cancer with asbestos exposure did not apply here. Those who dealt with mesothelioma did not demand epidemiological evidence. Their main problem was in agreeing that the tumor actually existed and how it should be defined. Pleural and abdominal cancers were sometimes mentioned in relation to asbestosis but until the report by Wagner, Sleggs and Marchand in 1960, this was not a major focus of research.

A review of opinions similar to that for lung cancer was done only by myself with the results shown in Table B. This shows that few authors ever expressed doubt about the relationship between this rare tumor and asbestos exposure and by 1953, the issue was fairly well resolved. A flood of articles following the appearance in 1960 of the paper by Wagner, Sleggs, and Marchand is apparent. In 1965, not a single writer expressed doubts about the relationship. Many did condition their opinions on the type of fiber involved, however, believing that crocidolite asbestos was most likely to be related to mesothelioma.

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Five Periods in Knowledge and Attitudes

In this literature review, I see five distinct periods in the development of knowledge and in attitudes about asbestos and lung cancer from the American point of view: The Pre-World War II period, characterized by a general rejection of a relationship; The Period 1939-45; characterized by a sharply divided opinion on the subject between German writers and the rest of the world; The Post-War World War II Period 1946-55, in which there was a gradual acceptance of a relationship first in England and then in America; The Period 1955-63, during which epidemiologists and biostatisticians entered the picture and demanded positive epidemiological evidence, and in which no further progress was made toward achieving a concensus; and The Period 1963-64, during which positive epidemiological studies coupled with positive animal studies largely ended the debate as to whether asbestos was a cause of cancer.

Key to Tables A and B

Code	Meaning
O	Original article (observations, studies, experiments.)
R	Review Article
E	Editorial
C	Communication (letters, etc.)
T	Textbook or Monograph
*	Foreign language article (not English)
a	Animal data
q	Quote from other source - no opinion expressed
f	Association depends on type of fiber
(name)	Author whose opinion is classified e.g. Article author (Discussant author) or Textbook Editor (Chapter author)
✓	Sarcoma only

Author's Last Name (O, a, f): indicates an original article on an animal study where the author expresses the opinion that the association is dependent on the type of fiber.

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Table A

Opinions of Authors Publishing 1933 - 1965
Regarding the Causal Relationship Between
Asbestos and Lung Cancer

Year	Definitely Causes Lung Cancer		Possibly Causes Lung Cancer		Unproven or Does not Cause Lung Cancer
	Without Asbestosis	Only After Asbestosis	Without Asbestosis	Only After Asbestosis	
1934					Wood {O}
1935				Lynch {O}	Gloyne {O}
1936				Egbert {O}	Gloyne {O}
1938		*Nordmann {O} *Hornig {O}		*Teleky {R} *Koelsch {R}	Vorwald {O, a} Brit. Med. J. {E} J.A.M.A. {E} Lanza (Gloyne) {T}
1939		*Bader {R}		Klotz {O} *Saupe {O}	Lynch {O} ILO {R} Lanza {T}
1940					Gardner {R}
1941	*Nordmann {O, a}	*Linzbach {O}		*Desmeules {O}	

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Table A (cont.)

Opinions of Authors Publishing 1933 - 1965
Regarding the Causal Relationship Between
Asbestos and Lung Cancer

Year	Definitely Causes Lung Cancer: Without Asbestosis	Definitely Causes Lung Cancer: Only After Asbestosis	Possibly Causes Lung Cancer: Without Asbestosis	Possibly Causes Lung Cancer: Only After Asbestosis	Unproven or Does not Cause Lung Cancer
1942		*Wegelin (R) *Welz (O)		Holleb (O) Hueper (T)	
1943		*Wedler (O) *Wedler (R) *Boemke (O) Hueper (R)		Homberger (O)	Wampler (T)
1946		Hueper (R) Hueper (R)			King (O, a)
1947				Kennaway (O)	*Wegelius (O)
1948		*Saita (R)		Lynch (O) Cureton (O)	Warren (R) Teleky (T)
1949		Merewether (O) Smith (R) Wyers (O) J.A.M.A. (E)		Doig (R)	
1951		Hueper (R) Owen (O, q) Stoll (O) Tabershaw (R)	Gloyne (O)		Vorwald (O, a) *Behrens (O, a) Sax (T)

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Table A (cont.)

Opinions of Authors Publishing 1933 - 1965
Regarding the Causal Relationship Between
Asbestos and Lung Cancer

Year	Definitely Causes Lung Cancer: Without Asbestosis	Definitely Causes Lung Cancer: Only After Asbestosis	Possibly Causes Lung Cancer: Without Asbestosis	Possibly Causes Lung Cancer: Only After Asbestosis	Unproven or Does not Cause Lung Cancer
1952		Smith {R} Hueper {R} Werber {O}		*Behrens {R}	Smith {R, a} Smith (Cartier) {O}
1953	IUAC {E}	Isselbacher {O} *Weiss {O} Smith {R} *Boemke{O}		Lynch {O}	
1955	Doll {O} Brit. M. J, {E} Lancet {E}	Hunter {q} Knox {C} *Rambola {O, f} *Porligiotti {O} Hueper {O} Bonser {O} Merewether {O} Hueper {R}	Breslow {O}	Lynch {O} Smith {R, f} *Jacob {O}	Cartier {O} Hueper {O, a}
1956		Weller {T} Hueper {R} *Bohlig {R}		Merewether {T} (Goldblatt) *Francia {O, f} McGee {q}	Rosenblatt {T} Todd {O} Mayer (Hammond) {T} *Bohlig {R}

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Table A (cont.)

Opinions of Authors Publishing 1933 - 1965
Regarding the Causal Relationship Between
Asbestos and Lung Cancer

Year	Definitely Causes Lung Cancer: Without Asbestosis	Definitely Causes Lung Cancer: Only After Asbestosis	Possibly Causes Lung Cancer: Without Asbestosis	Possibly Causes Lung Cancer: Only After Asbestosis	Unproven or Does not Cause Lung Cancer
1957		Jones-William {O} Fairhall {T, q} Lancet {E}		O'Donnell {O}	Sax {T} Lynch {O, a}
1958	*Schmahl {O, a, ✓}	Goldblatt {R} *Bohlig {O} *Chauvet{O}		Patty (Sander) {T}	Braun {O} *Bohlig {O}
1959	*Bohlig {O}	DuBois {T} Homberger (Hueper) {T} *Bohme {O} *Bohme {O} Eckardt {T}		*Nordvik {R, f}	
1960	Fleming (Schepers){T} Schilling (Gilson {T, f} *Konig {O}			Keal {O} Anderson {O}	Johnstone {T} Dunn {O}
1961		Heard {O} Teliachi {O} *Frankel {O} Trimble {C} *Krzymien {R}		*Sczymczykiewicz {R}	Johnstone {C}

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Table A (cont.)

Opinions of Authors Publishing 1933 - 1965
Regarding the Causal Relationship Between
Asbestos and Lung Cancer

Year	Definitely Causes Lung Cancer: Without Asbestosis	Definitely Causes Lung Cancer: Only After Asbestosis	Possibly Causes Lung Cancer: Without Asbestosis	Possibly Causes Lung Cancer: Only After Asbestosis	Unproven or Does not Cause Lung Cancer
1962			*Champeix {O} *DeLaguillaumie {O} Hunter {T}	Cordova {O} *Fingerland {O}	*Danrigal {O}
1963	Mancuso {O}	Leatheart{O} Castleman (Knowles) {O} Walters {O}		*Farina {O}	Lanza (Smith) {T}
1964	Doll {O} Elwood {O} Oettle {O} Selikoff {O}	*Noeninckx {O} Buchanan {O, f}		*Navratil {O} *Kogan {O} Gafafer {T}	Dis. of Chest {R, f}
1965	N. Eng. J. M. {E} IUAC {E}	Dutra {O} Elmes {O} Hinson {R} Jones-Williams {O} Can. M.A.J. {E} *Angpach {O}	Cauna {O}		Baum (Andrews) {T, q}

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Table B

Opinions of Authors Publishing 1933 - 1965 Regarding the Causal Relationship Between Asbestos Exposure and Mesothelioma

Definitely Causes Mesothelioma	Possibly Causes Mesothelioma	Unproven or Does Not Cause Mesothelioma
		Gloyne {O}
		Wood {O}
*Wedler {R} *Wedler {O}		
	Doig {R}	
		*Behrens {O, a}
	Smith {R}	Smith (Cartier) {R}
*Weiss {O}		
*Leicher {O}		
	Bonser {O}	
	*Bohlig {R}	
	*Van der Schoot {O}	
Schilling (Gilson) {T, f} Konig {O}	Keal {O} Wagner {O} Fleming (Schepers) {T, f}	
[illegible] {O} [illegible] {O}	Heard {O}	Knox {C}

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Table B (cont.)

Opinions of Authors Publishing 1933 - 1965
Regarding the Causal Relationship Between
Asbestos Exposure and Mesothelioma

Definitely Causes Mesothelioma	Possibly Causes Mesothelioma	Unproven or Does Not Cause Mesothelioma
McNutty {O, f} Thompson {O} Wagner {O, a} McCaughey {C} Enticknap {C}	Smither {C} Hunter {T}	
Leathart (Smither){R, f} Mancuso {O} Walters {R} Thomson {C} Lawson {C} Lawson {C}	Castleman {O} Thompson {O}	
Buchanan {O, f} Enticktap {O} Hourihane {O} *Noeninckx {O} Oettle {O} Owen {O} Smith {O, a}	Gafafer {T} Murray {R, f} Elwood {O, f} Fowler {O} Selikoff {O} Brit. Med. J. {E, f}	Dis. of Chest {R, f}
Dutra {O, q} Elmes {O} Hinson {R} Selikoff {O} Smith {O, a, f} Steel {O} *Anspach {O} N. Eng. J. M. {E} Can. M.A.J. {E, f} IUAC {E}		

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CONCLUSIONS

In Germany the question of whether asbestos caused lung cancer seemed to have been settled by the early 1940's. Asbestosis had been recognized for over 40 years. In 1934 in England, Wood and Gloyne reported two cases of lung carcinoma seen at autopsy in 43 cases of asbestosis, and in 1935 Gloyne gave a complete description of these two cases. Also in 1935, Lynch and Smith reported one case of lung cancer in an asbestosis case in the United States, and in 1936, Egbert and Geiger reported a case — also from the United States. In Germany, Nordmann added two cases of lung cancer in two cases of asbestosis, making a total of six and concluded, "A cause-effect correlation must be present here, even if I had been the only observer. We are indeed facing an occupational cancer which affects asbestos workers." German writers quickly accepted Nordmann's views. They were reinforced by an animal study in which Nordmann and Sorge reported pulmonary carcinomas in two white mice as the result of asbestos dust inhalation. Other German writers considered this experimental evidence needed for proof and gave Nordmann credit for discovering the relationship between asbestos and lung cancer. Meanwhile, in the United States, Hueper declared that, "Asbestosis cancer of the lung is the most recent newcomer among the occupational cancers of this organ." In 1950, West Germany declared cancer of the lung, when associated with asbestosis (of any degree), an occupational disease.

And yet, in the United States the question of asbestos and lung cancer remained unsettled. What prolonged the debate and when was the relationship finally accepted?

Gloyne, to whom credit for the discovery should really have gone, was extremely cautious in interpreting his findings. In his 1935 report,

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Gloyne quoted Bridge and Henry on conditions that must be fulfilled in order chat cancer be classified as industrial in origin: (a) that the incidence rate in the occupation under review should exceed that in the general population, to a significant extent, and (b) that in the occupation concerned, there should be sufficient association of the workers with a substance proved experimentally to have carcinogenic properties. In Gloyne's lifetime :hese conditions were not fulfilled. Nearly all the evidence dealt with the ssociation of asbestosis and cancer as seen at autopsy. In a paper published osthumously in 1951, Gloyne expressed concern for the selection obviously : work in picking cases for autopsy, pointing out that necropsy records at e London Chest Hospital showed 21.3% primary lung cancer whereas in the neral population, only 2.4% of deaths from all causes at ages 15 and over :e due to malignant disease of the lung.

Lynch, who actually got credit in the end, was no less skeptical. He concerned not only with the problem of selection but also with the lack experimental evidence. Only Nordmann and Sorge claimed to have produced :er experimentally with asbestos, while experiments by Vorwald and Karr, ; Clegg and Rae, Vorwald Durkan and Pratt, Behrens, and Hueper were tive. Moreover, W. E. Smith, in a review of animal work with asbestos, luded that the study by Nordmann and Sorge appeared to demonstrate that stos did not provoke lung tumors, since of the two tumors reported in stos-exposed animals, one was, based on photographs presented, merely a ous cell metaplasia, while the other, asserted to be an adenocarcinoma, type of tumor that can arise spontaneously from the mouse adenoma." Hueper seemed to agree with this and, outside of Germany, Smith's views rdmann's work gained some acceptance.

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Another problem in the United States was the attitude of leaders in the field of pneumoconiosis — particularly, Vorwald, Lanza, and Gardner. Their expressed concern was the lack of experimental data. In addition, the possibility of a different relationship between asbestosis and lung cancer as compared with silicosis and lung cancer must have been disturbing. Lanza was also concerned about the same selectivity that worried Gloyne and Lynch, and he wondered, in regard to English claims of an association in autopsied cases of asbestosis, how many cases of lung cancer would be found if lungs from any sort of population were subject to the same minute scrutiny.

The situation should have been resolved, from the American point of view, by a report by Merewether who, in 1949 compared lung or pleural cancer in cases of asbestosis reported for compensation with lung or pleural cancer in cases of silicosis. This was clearly the most important single study in bringing about a concensus in Great Britain. In America, however, this seems to have given birth to a new idea: there is a relationship between asbestosis and cancer in England and in Germany but not in the United States. This idea apparently originated with W. E. Smith; however, another Smith (K.W.) enlarged on this, stating that there was a difference due to the type of fiber used in England and Germany as compared with the United States. Italian writers picked this up as an argument for a difference between Italy and England. The argument was also repeated by Eckhardt, Gilson, and Johnstone and Miller.

There was no answer to the question of fiber type (or fiber contamination), and it no doubt delayed acceptance by those who were uncertain as to whether a problem truly existed in the United States. There was, however, an answer to the question of selection that so bothered Gloyne and Lynch. In 1955, an epidemiological study was reported of the type envisioned by

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ldge and Henry in which it was shown that the incidence of lung cancer in group of asbestos-exposed workers in England greatly exceeded that in a mparable group in the general population. This marked an end to a period en conclusions were based largely on pathological and clinical observations, l opened the door for contributions by biostatisticians and epidemiologists. probably also set back acceptance of a relationship between asbestos and ncer in the United States by another decade.

The epidemiologists demanded epidemiological evidence. In 1956, for mple, Hammond and Machle stated that with regard to a relationship ween asbestos and lung cancer "... there are at present too few cases and little epidemiologic data to establish a significant relationship." In 8, the Committee on Occupational Cancer of the AMA Council on Industrial lth concluded that individual case reports contribute little to an under- nding of occupational cancers and that "specific increases in age, sex, site-specific cancer incidence above normal incidences for the same age, , and site represent the only reliable evidence for the existence of an upational cancer hazard."

The first two epidemiological studies of this kind on asbestos and g cancer in North America in 1958 and 1960 were considered to be nega- e. Thus, as late as 1961, it could be said that "there is no epidemiological dence [of an association between asbestos and lung cancer] among American kers."

So what ended the debate in the United States? Probably three things: itive epidemiological studies in the United States in 1963 and 1964; a ely read 1960 study that showed that asbestos was associated with a rare cor -- malignant mesothelioma; and experimental evidence in 1962 and 1964 t asbestos had carcinogenic properties. So the kind of evidence demanded

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y Bridge and Henry, and which would have satisfied Gloyne, was finally eveloped 30 years after Gloyne made his initial observations, and over two ecades after the acceptance of a relationship between asbestos and lung ancer in Germany.

Clearly, the matter involved a question of what is acceptable and nclusive evidence. Perhaps a special set of rules are needed for relation-ips like asbestos and lung cancer where some other biologic response, such asbestosis, can be used as evidence of significant exposure, and the rules oposed by Bridge and Henry were not appropriate after all. Many writers re convinced of a relationship long before epidemiological and experimental idence was available. Aside from the high incidence of lung cancer in estotics, they were impressed by the predominance of cancer in the lower es, the time lapse between exposure and disease, the high incidence in ales, and the young age of many of the cases seen. Moreover, there were sonable theories regarding mechanisms by which asbestos could cause cancer. se arguments were seldom acknowledged by the epidemiologists and biostatis-ians.

In any event, the issue was definitely settled for the United States a conference on the Biologic Effects of Asbestos held in New York City 1964. At that conference additional epidemiologic evidence was presented, of 20 papers presented in which an opinion was expressed, none dissented a the view that asbestos is a cause of cancer.

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ABSTRACTS OF ORIGINAL ARTICLES
1934-65*

*Excluding papers presented at the Conference on the Biologic Effects of of Asbestos, New York City, October 1964.

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Date: 1934

Reference:

Wood, WB and Gloyne, SR: Pulmonary Asbestosis: A Review of One Hundred Cases, Lancet, 2, 1383 (1934)

Type of Cancer: Lung Cancer

Method of Study: Case Review

Population Examined: 100 asbestos workers seen as patients

Nature of Exposure: Occupational

Material: Not Given

Location: England (London)

Findings: Two Cases of Lung Cancer in 100 asbestos workers (autopsy)

Date: 1935

Reference:

Gloyne, SR: Two Cases of Squamous Carcinoma of the Lung Occurring in Asbestosis, Tubercle, 17, 5 (1935)

Type of Cancer: Lung Cancer

Method of Study: Case Report (2)

Population Examined: Autopsy Reports (2)

Nature of Exposure: Occupational - spinner and worker in mattress and opening departments of asbestos factory

Material: Not Given

Location: England (London)

Findings: Two cases of lung cancer in two cases of asbestosis (autopsy)

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Date: 1935

Reference:

Lynch, KM and Smith, WA: Pulmonary Asbestosis III: Carcinoma of the Lung in Asbesto Silicosis, Am J Cancer, 24, 56 (1935)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - asbestos mill weaver

Material: Not Given

Location: USA (South Carolina)

Findings: First recorded case (1) of lung cancer in a case of asbestosis in U.S.A. (autopsy)

Date: 1936

Reference:

Egbert, DS and Geiger, AJ: Pulmonary Asbestosis and Carcinoma: Report of a Case with Necropsy Findings, Am Rev Tuberc, 34, 143 (1936)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - weaver in an asbestos factory

Material: Not Given

Location: USA (Connecticut)

Findings: One case of lung cancer in one case of asbestosis (autopsy)

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Date: 1936

Reference:

Gloyne, SR: A Case of Oat Cell Carcinoma of the Lung Occurring in Asbestosis, Tubercle, 18, 100 (1936)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - packer in an asbestos works and then foremen in the stores department

Material: Not Given

Location: England (London)

Findings: One case of lung cancer in one case of asbestosis (autopsy)

Date: 1938

Reference:

Hornig, F: Klinische Betrachtungen zur Frage des Berufskrebses der Asbestarbeiter [Clinical Considerations on the Question of Occupational Cancer in Asbestos Workers], Ztschr Krebsforsch, 47, 281 (1938)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - worker in an asbestos factory

Material: Not Given

Location: Germany (Hannover)

Findings: One case of lung cancer in one case of asbestosis (autopsy)

Original Article: German

This case was also reported by Nordmann (1938)

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Date: 1938

Reference:

Nordmann, M: Der Berufskrebs der Asbestarbeiter [Occupational Cancer in Asbestos Workers], Ztschr Krebsforsch, 47, 288 (1938)

Type of Cancer: Lung Cancer

Method of Study: Case Reports (2)

Population Examined: Autopsy Reports (2)

Nature of Exposure: Occupational - worker in the spinning and weaving workshops, worker in pre-spinning workshop

Material: Not Given

Location: Germany (Hannover)

Findings: Two cases of lung cancer in two cases of asbestosis (autopsy)

Original Article: German

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Date: 1938

Reference:

Vorwald, AJ and Karr, JW: Pneumoconiosis and Pulmonary Carcinoma, Am J Path, 14, 49 (1938)

Type of Cancer: Lung Cancer

Method of Study:

1) Review of roentgenological reports throughout the world collected from literature.

2) Review of roentgenological survey of individuals examined at Saranac Laboratory.

3) Review of autopsy reports from literature.

4) Review of autopsy reports examined at Saranac Laboratory.

5)* Experimental Study (animal).

Population Examined: 235 Guinea pigs* exposed to asbestos (part 5 of Method of Study)

Nature of Exposure: Experimental* - heavy atmosphere concentrations

Material: Not Given

Location: U.S.A. (New York)

Findings: No pulmonary tumors observed in 235 guinea pigs exposed to high concentrations of asbestos dust.

*Only this area of the research isolates asbestos exposure.

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Date: 1939

Reference:

Klotz, MO: The Association of Silicosis and Carcinoma of the Lung, Am J Cancer, 35, 38 (1939).

Type of Cancer: Lung Cancer

Method of Study: Autopsy Survey

Population Examined: 50 silicotics (autopsy)

Nature of Exposure: Occupational

Material: Varied

Location: Canada

Findings: Four cases of lung cancer, none exposed to asbestos

Date: 1939

Reference:

Lynch, KM and Smith, WA: Pulmonary Asbestosis V: A Report of Bronchial Carcinoma and Epithelial Metaplasia, Am J Cancer, 36, 567 (1939).

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - weaver in an asbestos mill

Material: Not Given

Location: USA (South Carolina)

Findings: One case of lung cancer in a case of asbestosis (autopsy)

Note: Read before the American Society for Cancer Research, Richmond, VA April 5, 1939.

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Date: 1939

Reference:

Saupe, E: Weitere Beiträge zur Röntgendiagnose der Lungenasbestose [Further Contributions on the X-ray Diagnosis of Pulmonary Asbestosis], Arch Gewerbepath u Gewerbehyg, 9, 391 (1939)

Type of Cancer: Lung Cancer

Method of Study: X-ray Survey

Nature of Exposure: Occupational

Population Examined: 420 asbestos workers

Material: Not Given

Location: Germany (Dresden)

Findings: No lung cancer detected in 420 asbestos workers (X-ray)

Original Article: German

Date: 1941

Reference:

Desmeules, R, Rousseau, L, and Sirois, A: Amiantose et Cancers Pulmonaires [Asbestosis and Lung Cancer], Laval Med, 6, 79 (1941)

Type of Cancer: Lung Cancer

Method of Study: Case Reports (2)

Population Examined: Autopsy Reports (2)

Nature of Exposure: Occupational - a machine fitter in the asbestos industry; asbestos bagger

Material: Not Given

Location: Canada (Quebec)

Findings: Two cases of lung cancer in two cases of asbestosis (autopsy)

Original Article: French

CRMC-Motley1000-Subj-003043

Published by AsbestosClaims.Law
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Date: 1941

Reference:

Linzbach, AJ and Wedler, HW: Beitrag zum Berufskrebs der Asbestarbeiter [Contribution to the Occupational Cancer of Asbestos Workers], Arch Path Anat, 307, 387 (1941)

Type of Cancer: Lung Cancer

Method of Study: Case Reports (2)

Population Examined: Autopsy Reports (2)

Nature of Exposure: Occupational - worker in asbestos processing department; no details for second case

Material: Not Given

Location: Germany (Berlin)

Findings: Two cases of lung cancer in two cases of asbestosis (autopsy)

Original Article: German

Date: 1941

Reference:

Nordmann, M and Sorge, A: Lungenkrebs durch Asbestaub im Tierversuch [Lung Cancer Produced by Asbestos Dust in Animal Experiments], Ztschr Krebsforsch 51, 168 (1941)

Type of Cancer: Lung Cancer

Method of Study: Experimental (animal) Study

Population Examined: 100 white mice

Nature of Exposure: Experimental - dense clouds of asbestos dust for 6 to 13 weeks

Material: Chrysotile

Location: Germany (Hannover)

Findings: Two mice with carcinomas out of 10 mice surviving to 240 days

Original Article: German

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Date: 1942

Reference:

Holleb, HB and Angrist, A: Bronchogenic Carcinoma in Association with Pulmonary Asbestosis, Am J Path, 18, 123 (1942)

Type of Cancer: Lung Cancer

Population Examined: Autopsy Reports (2)

Method of Study: Case Reports (2)

Nature of Exposure: Occupational - employed to cover steam and water pipes with asbestos fabric; pipe coverer

Material: Not Given

Location: USA (New York)

Findings: Two cases of lung cancer in two cases of asbestosis (autopsy)

Date: 1942

Reference:

Welz, A: Weitere Beobachtungen über den Berufskrebs der Asbestarbeiter [Futher Observations of Occupational Cancer Among Asbestos Workers], Arch Gewerbepath u Gewerbehyg, 11, 536 (1942)

Type of Cancer: Lung Cancer

Method of Study: Case Reports (2)

Population Examined: Autopsy Reports (2)

Nature of Exposure: Occupational:

1. Worker in dust cleansing and dust preparation departments
2. Mixer in an asbestos plant - carding department

Material: Not Given

Location: Germany (Hannover)

Findings: Two cases of lung cancer in two cases of asbestosis (autopsy)

Original Article: German

CRMC-Motley1000-Subj-003045

Published by AsbestosClaims.Law
asbestosclaims.law/library/13129/100

Date: 1943

Reference:

Boemke, F: Asbestosis und Lungencarcinom [Asbestosis and Lung Carcinoma], Frankf Zeitschrift Path, 57, 569 (1943)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - carder in an asbestos factory

Material: Not Given

Location: Germany

Findings: One case of lung cancer in a case of asbestosis (autopsy)

Original Article: German

Date: 1943

Reference:

Homberger, F: The Co-Incidence of Primary Carcinoma of the Lungs and Pulmonary Asbestosis, Am J Path, 19, 797 (1943)

Type of Cancer: Lung Cancer

Method of Study: Case Reports (3)

Population Examined: Autopsy Reports (3)

Nature of Exposure: Occupational - workers (2) in asbestos factory; one exposure unknown

Material: Not Given

Location: USA (Connecticut)

Findings: Three cases of lung cancer in three cases of asbestosis (autopsy). In this laboratory four cases of lung cancer in eight cases of asbestosis seen over time.

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Date: 1943

Reference:

Wedler, HW: Über den Lungenkrebs bei Asbestose [Lung Cancer in Asbestosis Patients], Dtsch Arch Klin Med, 191, 189 (1943)

Type of Cancer: Lung Cancer and Pleural Cancer (also; stomach, esophagus and prostate cancer)

Method of Study*: Autopsy Review and Case Reports (3)

Population Examined*: Autopsy Reports

Source of Exposure*: Occupational

(1) worker in an asbestos plant
(2) worker in an asbestos rubber plant
(3) craftsman in an asbestos plant

Material*: Not Given

Location: Germany (Heidelberg)

Findings*: One case of lung cancer and two cases of pleural cancer in three cases of asbestosis (autopsy). Also, describes from world-wide literature 14 cases of lung and pleural cancer out of 92 cases of asbestosis (autopsy).

Original Article: German

Wedler reports three cases, observed by Bohme, Teutschlaeuder and Alwens, respectively, not previously reported.

CRMC-Motley1000-Subj-003047

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Date: 1946

Reference:

Fleischer, WE, Frederick, JV, Gade, RL, and Drinker, P: A Health Survey of Pipe Covering Operations in Constructing Naval Vessels, J Ind Hyg and Toxic, 28, 9 (1946)

Type of Cancer: —

Method of Study: X-ray Survey

Population Examined: 1074 pipe coverers in two government navy yards and in two navy contract yards

Nature of Exposure: Occupational - pipe coverers exposed to varied amounts of asbestos dust

Material: Amosite (44 - 57%) and chrysotile (6 - 43%)

Location: USA

Findings: Three cases of asbestosis in 1074 pipe coverers (no cancer observed)

Date: 1946

Reference:

King, EJ, Clegg, JW and Rae, VM: The Effect of Asbestos, and of Asbestos and Aluminium, on the Lungs of Rabbits, Thorax, 1, 188 (1946)

Type of Cancer: No cancer mentioned

Method of Study: Experimental (animal) Study

Population Examined: 40 rabbits

Nature of Exposure: Experimental - intertracheal administration

Group 1: 12 rabbits; long-fibre asbestos

Group 2: 12 rabbits; long-fibre asbestos and aluminium

Group 3: 7 rabbits; short-fibre asbestos

Group 4: 9 rabbits; short-fibre asbestos and aluminium

Material: Rhodesian asbestos

Location: England (London)

Findings: No cancer in 40 rabbits after intertracheal administration of asbestos

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Date: 1947

Reference:

Kennaway, EL and Kennaway, NM: A Further Study of the Incidence of Cancer of the Lung and Larynx, Brit J Cancer, 1, 260 (1947)

Type of Cancer: Lung Cancer

Method of Study: Survey of Death Certificates

Population Examined: Death certificates of cases of lung cancer and larynx cancer in males from England and Wales for 1921 through 1938

Nature of Exposure: Unknown

Material: Unknown

Location: England (London)

Findings: Eight cases of lung cancer in asbestos workers dying 1934 to 1938 (Death Certificates)

Date: 1947

Reference:

Wegelius, C: Changes in the Lungs in 126 Cases of Asbestosis Observed in Finland, Acta Radiol, 28, 1939 (1947)

Type of Cancer: Lung Cancer

Method of Study: Roentgenological Survey

Population Examined: Occupational; 476 workers, 126 with asbestosis

Nature of Exposure: 34 workers in dressing works (at asbestos mine); 92 in factory for finished products

Material: Not Given

Location: Finland

Findings: No lung cancer in 476 asbestos workers, 126 with asbestosis (roentgenological)

Original Article: Finnish

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Date: 1948

Reference:

Cureton, RJR: Squamous Cell Carcinoma Occurring in Asbestosis of the Lung, Brit J Cancer, 2, 249 (1948)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - worker in a factory making asbestos pipe covers

Material: Not Given

Location: England (London)

Findings: One case of lung cancer in one case of asbestosis (autopsy)

Date: 1948

Reference:

Lynch, KM and Cannon, WM: Asbestosis VI: Analysis of Forty Necropsied Cases, Dis Chest, 14, 874 (1948)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1 new case)

Population Examined: Autopsy Report (1)

Nature of Exposure: Not Given

Material: Not Given

Location: USA (South Carolina)

Findings: One case of lung cancer in one case of asbestosis (autopsy). In this laboratory, 3 cases of lung cancer out of 40 cases of asbestosis over 18 years.

Note: Presented at 13th Annual Meeting, American College of Chest Physicians, Atlantic City, NJ, June 8, 1947.

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Date: 1949

Reference:

Wyers, H.; Asbestosis; Post Grad M J, 25, 631 (1949)

Type of Cancer: Lung Cancer and Cancer of Other Organs

Method of Study: Autopsy Survey

Population Examined: Autopsy reports on 115 deaths from asbestosis

Nature of Exposure: Occupational - Workers from a company engaged in the manufacturing of asbestos products (see Smith 1952)

Material: Not Given (in article) - blue asbestos (crocidolite) South Africa (Smith - '52)

Location: England

Findings: 17 cases of lung cancer and 7 cases of cancer of other organs in 115 cases of asbestosis (autopsy)

Note: These lung cancers are included in those reported by Merewether 1949 (see Smith 1952)

Date: 1949

Reference:

Merewether, ERA: Annual Report of the Chief Inspector of Factories for the Year 1947, H.M.S.O., London, 1949

Type of Cancer: Lung Cancer

Method of Study: Autopsy Survey

Population Examined: 235 cases (deaths) from asbestosis from 1924 to 1946

Nature of Exposure: Occupational

Material: Not given

Location: England (London)

Findings: 31 cases of lung cancer in 235 cases of asbestosis

CRMC-Motley1000-Subj-003051

Date: 1951

Reference:

Behrens, W: Über Experimentelle Asbestosis [Experimental Asbestosis], Schweiz z Path, 14, 275 (1951)

Type of Cancer: No cancer mentioned

Method of Study: Experimental Study (animal)

Population Examined:

a. 92 mice
b. 15 mice
c. 11 rats

Nature of Exposure: Experimental
a. 10-20mg asbestos/cc injected intraperitoneally
b. 1/2 cc asbestos (above) + 1/2 cc human citrate blood injected intraperitoneally
c. 15 mg asbestos/cc intratracheally instilled

Material: Chrysotile

Location: Switzerland (Zurich)

Findings: No cancer observed

Original Article: German

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Date: 1951

Reference:

Gloyne, SR: Pneumoconiosis: A Histological Survey of Necropsy Material in 1205 Cases, Lancet, 1, 810 (1951)

Type of Cancer: Lung Cancer

Method of Study: Autopsy Survey

Population Examined: 1,205 lungs (or portions of lungs), 1,036 with pneumoconiosis (121 asbestos workers - Smith 1952)

Nature of Exposure: Not Given

Material: Not Given (Rhodesian and South African blue asbestos - Smith '52)

Location: England

Findings: 17 cases of lung cancer in 121 cases of asbestosis (Necropsy)

Note: The 17 cases of coexistent lung cancer and asbestosis are those reported by Wyers. (see: Smith 1952)

Date: 1951

Reference:

Owen, TK: Carcinoma and Asbestosis of the Lung: Report of a Case, Brit J Cancer, 5, 382 (1951)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - worker in asbestos factory

Material: Not Given

Location: England (London)

Findings: One case of lung cancer in one case of asbestosis (autopsy)

Quotes personal opinion of M. L. Stewart

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Date: 1951

Reference:

Stoll, R, Bass, R and Angrist, AA: Asbestosis Associated with Bronchogenic Carcinoma, Arch Intern Med, 88, 831 (1951)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - pipe coverer (asbestos)

Material: Not Given

Location: USA (New York)

Findings: One case of lung cancer in one case of asbestosis (autopsy)

Date: 1951

Reference:

Vorwald, AJ, Durkan, TM and Pratt, PC: Experimental Studies of Asbestosis, Arch Ind Hyg & Occup Med, 3, 1 (1951)

Type of Cancer: Lung Cancer

Method of Study: Experimental Study (animal)

Population Examined: 100 or more Guinea pigs and sometimes smaller numbers of rabbits, cats, dogs, rats or mice.

Nature of Exposure: Experimental

a. Inhalation: high concentration in atmosphere.

b. Injection: dust, dry or suspended in fluid, injected into animal by the intravenous, the intraperitoneal, the intratracheal or another route.

Material: Chrysotile

Location: USA (New York)

Findings: No lung cancer observed in various animals exposed to asbestos dust.

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Date: 1952

Reference:

Werber, M: Lungen-Asbestose und Karzinom [Pulmonary Asbestosis and Carcinoma], Z. Arbeitsmed u Arbeitsschutz, 2, 179 (1952)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: X-ray Report and Thoractomy Report (1)

Nature of Exposure: Occupational - asbestos plant owner

Material: Not Given

Location: Germany (Todtmoos/Schwarzwald)

Findings: One case of lung cancer in a case of asbestosis (X-ray and Thoractomy)

Original Article: German

Date: 1953

Reference:

Boemke, F: Das Lungenkarzinom in der Asbeststaublunge [Lung Carcinoma in Patients Suffering from Asbestos Pneumoconiosis], Med Mschr, 7, 77 (1953)

Type of Cancer: Lung Cancer

Method of Study: Case Reports (3)

Population Examined: Autopsy Reports (3)

Nature of Exposure: Occupational
(1) Carder in an asbestos plant
(2) Operator of a tearing machine in an asbestos plant
(3) Employee in an asbestos plant

Material: Not Given

Location: Germany

Findings: Three cases of lung cancer in three cases of asbestosis (autopsy)

Original Article: German

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Date: 1953

Reference:

Weiss, A: Pleurakrebs bei Lungenasbestose in Vivo Morphologisch Gesichert [Morphological Substantiation in Vivo of Cancer of the Pleura in a Case of Asbestosis], Medizinische, 1, 93 (1953)

Type of Cancer: Cancer of the Pleura

Method of Study: Case Report (1)

Population Examined: Thoracoscopy and Biopsy Report (1)

Nature of Exposure: Occupational - worker at a naval dockyard on insulation for pipes and valve systems

Material: Not Given

Location: Germany

Findings: One case of pleura cancer in a case of asbestosis (Thoracoscopy and biopsy)

Original Article: German

Date: 1954

Reference:

Leicher, F: Primärer Deckzellantumor Des Bauchfells Bei Asbestose [Primary Epithelial Tumor of the Peritoneum in Asbestosis], Arch Gewerbepath u Gewerbehyg, 13, 382 (1954)

Type of Cancer: Cancer of the Peritoneum

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - yarn and asbestos spinner

Material: Not Given

Location: Germany

Findings: One case of cancer of peritoneum and asbestosis of the lungs

Original Article: German

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Date: 1955

Reference:

Bonser, GM, Faulds, JS and Stewart, MJ: Occupational Cancer of the Urinary Bladder in Dyestuffs Operatives and of the Lung in Asbestos Textile Workers and Iron Ore Miners, Am J Clin Path, 25, 126 (1955)

Type of Cancer: Cancer of the Lung, Pleura, and Peritoneum

Method of Study: Autopsy Survey

Population Examined: 72 cases of asbestosis - autopsy reports from 1928

Nature of Exposure: Occupational - workers in two asbestos factories

Material: Not Given

Location: England (Carlisle)

Findings: 12 cases of lung cancer, 2 cases of pleura cancer, and 4 cases of Peritoneal cancer in 72 cases of asbestosis (autopsy)

Date: 1955

Reference:

Breslow, L: Industrial Aspects of Bronchogenic Neoplasms, Dis Chest, 28, 421 (1955)

Type of Cancer: Lung Cancer

Method of Study: Case - Control (Retrospective)

Population Examined: 518 lung cancer patients; 518 matched controls in 11 hospitals

Nature of Exposure: Occupational

Material: Unknown

Location: USA (California)

Findings: 10 lung cancer patients out of 518 employed at least 5 years as steamfitters, boiler makers, asbestos workers as compared to one (1) control (non lung cancer) out of 518.

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Reference:

Cartier, P: Some Clinical Observations of Asbestosis in Mine and Mill Workers, Arch Ind Health, 11, 204 (1955)

Type of Cancer: Lung Cancer

Method of Study: X-ray survey and Autopsy survey

Population Examined: 4000 asbestos mining workers

Nature of Exposure: Occupational - workers at the Thetford Mines, Quebec

Material: Not Given

Location: Canada (Quebec)

Findings: 6 cases of lung cancer in 40 autopsied cases of asbestosis and 7 cases of lung cancer in workers without asbestosis.

Note: Read in the Symposium on Occupational Diseases of the Lungs; Mass. Med. Soc. and Inst. of Industr. Med. of New York Univ. Post-Grad. Med. School; October, 1955

Date: 1955

Reference:

Doll, R: Mortality from Lung Cancer in asbestos workers, Brit J Ind Med, 12, 81 (1955)

Type of Cancer: Lung Cancer; Pleura Cancer

Method of Study:

a. Survey of Autopsy Records
b. Epidemiologic Study

Population Examined:

a. 105 consecutive autopsy records of persons known to have been employed at a large asbestos works.

b. 113 men who had worked for at least 20 years in places of high dust exposure.

Nature of Exposure: Occupational - employees at asbestos works

Material: Not Given

Location: England

Findings:

a. 15 lung cancer (includes one pleura cancer) in association with asbestosis. 3 lung cancer with no asbestosis.

b. 11 lung cancer observed; 0.8 expected.

Date: 1955

Reference:

Jacob, G and Bohlig, H: Über Häufigkeit und Besonderheiten des Lungenkrebses bei Asbestose [On the Incidence and Features of Lung Cancer in Asbestosis], Arch Gewerbepath u Gewerbehyg, 14, 10 (1955)

Type of Cancer: Lung Cancer

Method of Study: Case Review

Population Examined: 343 cases of asbestosis

Nature of Exposure: Occupational - two asbestos weavers, one asbestos puncher and a pulper and spinner of asbestos

Material: Not Given

Location: Germany (Dresden)

Findings: Four cases of lung cancer in 343 cases of asbestosis (autopsy)

Original Article: German

Date: 1955

Lynch, KM and Pratt-Thomas, HR: Carcinoma of the Lung in Asbestosis: Report of Two additional Cases, Southern Med J, 48, 565 (1955)

Type of Cancer: Lung Cancer

Method of Study: Case Reports (2)

Population Examined: Autopsy series of 49 cases of asbestosis

Nature of Exposure: Occupational - labor foreman; spinner in asbestos plant

Material: Not Given

Location: USA

Findings: 4 cases of cancer in 49 cases of asbestosis - (autopsy) [See discussion on opinion in industrial compensation case] Two case reports - part of 4.

Note: Read before the Section on Pathology, Southern Med. Assoc., 48th Annual Meeting, St. Louis, MO; November, 1954.

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Date: 1955

Reference:

Merewether, ERA: Annual Report of the Chief Inspector of Factories for the Year 1954, H.M.S.O., London, 1955

Type of Cancer: Lung Cancer - Cancer Other Sites

Population Examined: 344 cases (deaths) from asbestosis collected from 1924 thru 1954

Nature of Exposure: Occupational

Material: Not Given

Location: England (London)

Findings: 55 cases of lung cancer, 11 cases of cancer of other sites (not specified) in 344 cases of asbestosis (autopsy)

Date: 1955

Reference:

Portigliati-Barbos, M: Considerazoni Sull' Associazione: Asbestosi e Carcinoma Polmonare [Observations on the Association of Asbestosis and Lung Cancer], Giorn della Accad Med Torino, 115, 91 (1955)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - spinner in an asbestos textile factory

Material: Not Given

Location: Italy (Turin)

Findings: One case of lung cancer in a case of asbestosis (autopsy)

Original Article: Italian

Date: 1955

Reference:

Rambola, G: Asbestosi Carcinoma Polmonare in una Filatrice Di Amianto (Spunti Sul Problema Ocogeno Dell' Asbesto) [Asbestosis and Pulmonary Carcinoma in a Female Asbestos Spinner (Remarks on the Oncogenic Problem of Asbestos)], Med d Lavoro, 46, 242 (1955)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - spinner in an asbestos factory

Material: Chrysotile

Location: Italy (Milan)

Findings: One case of lung cancer in a case of asbestosis (autopsy) [Italy's first reported case]

Original Article: Italian

Date: 1956

Reference:

Francia, A and Monarca, G: Asbestosi e Carcinoma Pulmonare [Asbestosis and Pulmonary Carcinoma], Minerva Med, 47, 1950 (1956)

Type of Cancer: Lung Cancer; Pleura Cancer (mesothelioma)

Method of Study: Case Reports (2)

Population Examined: X-ray Report (1), Autopsy Report (1)

Nature of Exposure: Occupational - welder in an asbestos plant; worker in an asbestos processing firm

Material: Not Given (Probably Chrysotile)

Location: Italy (Turin)

Findings: One case of lung cancer in a case of asbestosis (X-ray)
One case of pleural mesothelioma in a case of asbestosis (autopsy)

Original Article: Italian

Date: 1956

Reference:

Todd, TC: MacDermot, HE and Mathews, WH: Clinico-Pathological Conference VII [Montreal General Hospital], Canad M.A.J., 75, 757 (1956)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - worker in asbestos mines

Material: Not Given

Location: Canada (Montreal)

Findings: One case of lung cancer in one case of asbestosis (autopsy)

Date: 1957

Reference:

Jones-Williams, W: Alveolar Metaplasia: Its Relationship to Pulmonary Fibrosis and the Development of Lung Cancer, Brit J Cancer, 11, 30 (1957)

Type of Cancer: Lung Cancer

Method of Study: Review of Lungs (Lung parts)

Population Examined: 60 lungs of asbestos workers

Nature of Exposure: Occupational: asbestos workers

Material: Not Given

Location: Wales

Findings: Thirteen cases of lung cancer in sixty unselected lungs of asbestos workers

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Date: 1957

Reference:

Lynch, KM, McIver, FA and Cain, JR: Pulmonary Tumors in Mice Exposed to Asbestos Dust, Arch Ind Health, 15, 207 (1957)

Type of Cancer: Lung Cancer

Method of Study: Experimental (Animal Study)

Population Examined: 776 mice in test and control groups - post mortems
349 mice studied at 19 and 24 months

Nature of Exposure: Experimental - high atmospheric concentrations

Material: Asbestos Floats 7-TF-2 (Chrysotile)

Location: USA (South Carolina)

Findings: Test: 46% with lung tumors, 18% with multiple tumors.
Control: 36% with lung tumors, 8% with multiple tumors.
No malignant tumors found in either group.

Date: 1957

Reference:

O'Donnell, WM and Mann, RH: Asbestos: An Extrinsic Factor in the Pathogenesis of Bronchogenic Carcinoma [Abst. of presentation]: Am J Path, 33, 610 (1957)

Type of Cancer: Lung Cancer

Method of Study: Autopsy Survey

Population Examined: 27 cases of asbestosis

Nature of Exposure: Occupational - employees at asbestos textile mill

Material: Not Given

Location: USA (Pennsylvania)

Findings: 13 cases of lung cancer in 27 cases of asbestosis (autopsy)

Note: Presented at the American Association of Pathologists and Bacteriologist: 54th Annual Meeting; Symposium on Diseases Caused by Environmental Facto· Washington, D.C., April 1957.

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Date: 1958

Reference:

Bohlig, H and Jacob, G: Die Haufigkeit des Lungenkrebses bei Deutschen Asbestarbeitern [Incidence of Lung Cancer Among German Asbestos Workers], Dtsch Gesundheit, 13, 1101 (1958)

Type of Cancer: Lung Cancer

Method of Study: Case Review

Population Examined: 517 asbestosis cases

Nature of Exposure: Occupational

Material: Not Given

Location: Germany (Dresden)

Findings: Five cases of lung cancer in 517 asbestosis cases (eleven autopsies)

Original Article: German

Date: 1958

Reference:

Braun, DC and Truan, TD: An Epidemiological Study of Lung Cancer in Asbestos Miners, Arch Ind Health, 17, 634 (1958)

Type of Cancer: Lung Cancer

Method of Study: Epidemiological Study

Population Examined: 5958 workers (miners) from Thetford Mines and Asbestos, Que. who had 5 or more years of exposure and were on employment rolls in 1950. Followed 1950 through 1955.

Nature of Exposure: Occupational - asbestos miners

Material: Chrysotile

Location: Canada (Quebec)

Findings: 9 "proved" cancer of lung in cohort; (4 with asbestosis); 6 expected cases (from figures of Province of Quebec 1954, 1955)

Date: 1958

Reference:

Chauvet, M: Asbestose et Cancer Bronchique [Asbestosis and Bronchial Cancer], La Presse Med, 21, 908 (1958)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - worker in preparation of circular joints from asbestos

Material: Not Given

Location: Switzerland (Geneva)

Findings: One case of lung cancer in one case of asbestosis (autopsy)

Original Article: French

Date: 1958

Reference:

Schmähl, D: Cancerogene Wirkung von Asbest bei Implantation an Ratten [Carcinogenic Effect of Asbestos Implantation in Rats], Ztschr Krebsforsch, 62, 561 (1958)

Type of Cancer: Lung Cancer

Method of Study: Experimental Study (animal)

Population Examined: 39 rats

Nature of Exposure: Experimental; subcutaneous and intraperitoneal implantation of asbestos in fiber or fragment form.

Material: Not Given

Location: Germany

Findings: Eleven of the 30 rats that survived longer than 15 months developed sarcomas at the site of implantation

Original Article: German

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Date: 1958

Reference:

Van der Schoot, HCM: Asbestosis en Pleuragezwellen [Asbestosis and Tumors of the Pleura[. Med T. Geneesk, 102, 1125 (1958) _

Type of Cancer: Pleural Cancer (mesothelioma) (also peritoneal mesothelioma: see discussion)

Method of Study: Case Reports (3)

Population Examined: Autopsy Reports (3)

Nature of Exposure: Occupational - insulators who worked with asbestos

Material: Not Given

Location: Netherlands

Findings: Three cases of pleural mesothelioma in three cases of asbestosis (autopsy)

Original Article: Dutch

Date: 1959

Bohlig, H, Jacob, G and Kallabis, B: Über Morbidital und Pathologie Asbestlungenkrebses [Morbidity and Pathology of Lung Cancer due to Asbestos], Ztsch Unfallmed u Berifskrank, 52, 64 (1959)

Type of Cancer: Lung Cancer

Method of Study: Case Review

Population Examined: 517 asbestosis patients

Nature of Exposure: Occupational

Material: Not Given

Location: Germany (Dresden)

Findings: Five cases of lung cancer in 517 asbestosis patients (eleven autopsies

Original Article: German

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Date: 1959

Reference:

Bohme, A: Asbestose und Lungencarcinom I [Asbestosis and Carcinoma of the Lung], Arch Gewerbepath u Gewerbehyg, 17, 384 (1959)

Type of Cancer: Lung Cancer

Method of Cancer: Case Reports (6)

Population Examined: Autopsy Reports (6)

Nature of Exposure: Occupational

1. Master weaver
2. Work in carding room; later, a foreman
3. Bricklayer in asbestos factory
4. Worker in carding department; later, a master spinner
5. Carder, spinner and weaver of asbestos
6. Work in carding; later, a foreman

Material: Not Given

Location: Germany

Findings: Six cases of lung cancer in six cases of asbestosis (autopsy)

Original Article: German

Date: 1959

Reference:

Bohme, A: Asbestose and Lungencarcinom II [Asbestosis and Carcinoma of the Lung], Arch Gewerbepath u Gewerbehyg, 17, 457 (1959)

Type of Cancer: Lung Cancer, stomach cancer and pancreas cancer

Method of Study: Review of Insurance Records

Population Examined: Insurance records of 125 asbestos workers whose diseases were compensable

Nature of Exposure: Occupational

Material: Not Given

Findings: Fifteen cases of lung cancer, one case of stomach cancer, one case of pancreas cancer in 31 deaths of workers with asbestosis out of 125 compensated asbestos workers (autopsy)

Original Article: German

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Date: 1960

Reference:

Anderson, J and Campagna, FA: Asbestosis and Carcinoma of the Lung: Case Report and Reviews of the Literature, Arch Env Health, 1, 27 (1960)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - asbestos insulator

Material: Not Given

Location: USA (San Francisco)

Findings: One case of lung cancer in one case of asbestosis (autopsy)

Date: 1960

Reference:

Dunn, JE, Linden, G and Breslow, L: Lung Cancer Mortality Experience of Men in Certain Occupations in California, Am J Pub Health, 50, 1475 (1960)

Type of Cancer: Lung Cancer

Method of Study: Epidemiological Study

Population Examined: 7,836 asbestos workers - Followed 1954-1958

Nature of Exposure: Occupational

Material: Not Given

Location: USA (California)

Findings: Preliminary report, only 4 years follow-up. 19 cases of lung cancer observed, 13.7 expected cases based on controls (death certificates).

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Date: 1960

Reference:

Keal, EE: Asbestosis and Abdominal Neoplasms, Lancet, 2, 1211 (1960)

Type of Cancer: Cancer of Lung and Abdomen

Method of Study: Hospital Records Survey

Population Examined: 42 cases of asbestosis from hospital records

Nature of Exposure: Occupational - 37 asbestos workers, 5 unspecified

Material: Not Given

Location: England (Leeds)

Findings: 14 cases of lung cancer, 10 cases of ovarian or peritoneal cancer in 42 cases of asbestosis (autopsy).

Date: 1960

Reference:

Konig, J: Über die Asbestose [Asbestosis], Arch Gewerbepath u Gewerbehyg, 18, 159 (1960)

Type of Cancer: Lung Cancer & Pleural Cancer (and other cancers)

Method of Study: Autopsy Survey

Population Examined: Autopsy Reports - 36 cases of asbestosis

Nature of Exposure: Occupational - 20 cases, Unknown - 16 cases

Material: Not Given

Location: Germany (Hamburg)

Findings: Seven cases of lung cancer, four cases of pleural cancer, four cases of stomach cancer, three cases of peritoneal cancer, one case of esophageal cancer, one case of pancreas cancer, one case of bladder cancer and one case of cancer of the sigmoid colon in 36 cases of asbestosis (autopsy)

Original Article: German

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Date: 1960

Reference:

Wagner, JC, Sleggs, CA and Marchand: Diffuse Pleural Mesothelioma and Asbestos Exposure in the North Western Cape Province, Brit J Ind Med, 17, 260 (1960)

Type of Cancer: Pleura Cancer (mesothelioma)

Method of Study: Autopsy Survey

Population Examined: Autopsy Reports

Nature of Exposure: Occupational and Environmental

Material: Crocidolite (Cape Blue Asbestos)

Location: South Africa (North Western Cape Province)

Findings: 33 cases of diffuse pleural mesothelioma - 32 have a probable exposure to asbestos, 8 cases with asbestosis (autopsy)

Date: 1961

Reference:

Frankel, M and de Jager, H: Mesothelioma Peritonei in Asbestosis Pulmonum, Jaarboek van Kankeronderyoek en Kankerbestrijding, 11, 99 (1961)

Type of Cancer: Mesothelioma of the Peritoneum

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - insulator

Material: Not Given

Location: Netherlands

Findings: One case of mesothelioma of the peritoneum in a case of asbestosis (autopsy)

Original Article: Dutch

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Date: 1961

Reference:

Heard, BE and Williams, R: The Pathology of Asbestosis with Reference to Lung Function, Thorax, 16, 264 (1961)

Type of Cancer: Lung Cancer and Peritoneal Cancer (Mesothelioma)

Method of Study: Case Reports

Population Examined: 6 cases of asbestosis

Nature of Exposure: Occupational

Material: Not Given

Location: England (London)

Findings: 3 cases of lung cancer and one case of mesothelioma of the peritoneum in six cases of asbestosis (autopsy)

Date: 1961

Reference:

Sleggs, CA, Marchand, P and Wagner, JC: Diffuse Pleural Mesothelioma in South Africa, S Afr Med J, 35, 28 (1961)

Type of Cancer: Pleura Cancer (Mesotheliomas)

Method of Study: Lung Survey (histological)

Population Examined: Lungs examined over 4 years

Nature of Exposure: Occupational and Environmental

Material: Crocidolite

Location: South Africa (Johannesburg)

Findings: 34 cases of pleural mesothelioma. Asbestos bodies in lung tissue of 30% (biopsy)

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Date: 1961

Reference:

Telischi, M and Rubenstone, AI: Pulmonary Asbestosis Associated with Primary Carcinoma of the Lung, Bronchial Adenomas and Adenocarcinoma of the Stomach, Arch Path, 72, 234 (1961)

Type of Cancer: Lung Cancer and Stomach Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - plaster mixer

Material: Not Given

Locations: USA (Chicago)

Findings: One case lung cancer, bronchial adenomas and stomach cancer in one case asbestosis (autopsy)

Date: 1962

Reference:

Champeix, J, De Laguillaumie, B, Jacquemet, L, Mory, F and Geille, A: Cancer Bronchique et Exposition aux Poussieres D'Amiante [Bronchial Cancer and Exposure to Asbestos Dust], Arch Mal Prof, 23, 267 (1962)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Surgery and Autopsy Report

Nature of Exposure: Occupational - worker in an asbestos factory warehouse

Material: Not Given

Location: France (Puy-de-Dome)

Findings: One case of lung cancer in one case of asbestosis (surgery-autopsy)

Original Article: French

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Date: 1962

Reference:

Cordova, JF, Tesluk, H and Knudtson, KP: Asbestosis and Carcinoma of the Lung, Cancer, 15, 1181 (1962)

Type of Cancer: Lung Cancer

Method of Study: Case Reports (11)

Population Examined: Surgical and Autopsy Reports (11)

Nature of Exposure: Occupational

Material: Not Given

Location: USA (Washington)

Findings: Eleven cases of lung cancer in eleven cases of asbestosis (autopsy and surgery)

Date: 1962

Reference:

Danrigal, A, Tabbara, W, Proteau, J and Dérobert, L: Asbestose, Tuberculose Pulmonaire Opéreé et Cancer du Poumon [Asbestosis, Surgically Treated Pulmonary Tuberculosis and Cancer of the Lung], Ann Med Legale, 42, 69 (1962)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational

Material: Not Given

Location: France

Findings: One case of lung cancer in a case of asbestosis - tuberculosis (autopsy)

Original Article: French

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Date: 1962

Reference:

DeLaguillaumie, B, Champiex, J, and Jacquemet, LR: Relations Entre Cancers Bronchiques et Asbestose [Relationships between Bronchial Cancers and Asbestosis], Arch Anat Path, 10, 144 (1962)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Surgery and Autopsy Report

Nature of Exposure: Occupational - worker in an asbestos factory warehouse

Material: Not Given

Location: France (Puy-de-Dome)

Findings: One case of lung cancer in one case of asbestosis (surgery-autopsy)

Original Article: French

This is the same case reported by Champeix et al (1962)

Date: 1962

Reference:

Fingerland, A and Jindrichova, J: Asbestosis of the Lungs Associated with Lung Cancer, Prac Lek, 14, 468 (1962)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - rolling asbestos plates

Material: Not Given

Location: Czechoslovakia

Findings: One case of lung cancer in a case of asbestosis (autopsy)

Original Article: Czechoslovakian

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Date: 1962

Reference:

McCaughey, WTE, Wade, OL and Elmes, PC: Exposure to Asbestos Dust and Diffuse Pleural Mesothelioma [Correspondence], Brit Med J, 2, 1397 (1962)

Type of Cancer: Cancer of Pleura (Mesothelioma)

Method of Study: Correspondence - Case Reports

Population Examined: 15 cases (lung sections) of pleural mesothelioma

Nature of Exposure: Occupational: asbestos processing and shipyards work (accounted for 10 of the 15 cases)

Material: Not Given

Location: Ireland (Belfast)

Findings: 15 cases of pleural mesothelioma, 12 of which had asbestos bodies in lungs

Date: 1962

Reference:

McNulty, JC: Malignant Pleural Mesothelioma in an Asbestos Worker, M J Australia, 2, 953 (1962)

Type of Cancer: Pleural Cancer (Mesothelioma)

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - mill worker in an asbestos mine

Material: Crocidolite

Location: Western Australia

Findings: One case of pleural mesothelioma in a case of asbestosis (autopsy)

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Date: 1962

Reference:

Thompson, JC: Mesothelioma of Pleura or Peritoneum and Limited Basal Asbestosis, S Afr Med J, 36, 759 (1962)

Type of Cancer: Cancer of Pleura and Cancer of Peritoneum (Mesothelioma)

Method of Study: Case Reports (7)

Population Examined: Autopsy Reports (7)

Nature of Exposure: Occupational - one case; Unknown - 6 cases

Material: Not Given

Location: South Africa (Cape Town)

Findings: 7 cases of mesothelioma, 4 in pleura and 3 in peritoneum. None had asbestosis clinically; at autopsy lungs did not show the appearances of asbestosis. 6 of the cases had pulmonary asbestosis, determined microscopically, only in basal 1 cm of lower lobes.

Note: Abstract of a paper presented at the Research Forum, University of Cape Town, on 14 June, 1962.

Date: 1962

Reference:

Wagner, JC: Experimental Production of Mesothelial Tumours of the Pleura by Implantation of Dusts in Laboratory Animals, Nature, 196, 180 (1962)

Type of Cancer: Pleura Cancer (Mesothelioma)

Method of Study: Experimental Study (animal)

Population Examined: 106 rats

Nature of Exposure: Experimental - dusts were ground, suspended in normal saline and injected into the pleural cavities of the rats.

Material: Crocidolite fiber, Crocidolite ore, Chrysotile, Amosite and other materials.

Location: South Africa (Johannesburg)

Findings: 2 out of 20 rats injected with crocidolite fiber (ground) and 1 out of 20 rats injected with chrysotile developed pleural mesotheliomas; also one rat surviving a chrysotile dusting later died of pleural mesothelioma.

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Date: 1963

Reference:

Lawson, JP: Exposure to Asbestos Dust [Correspondence], Brit Med J, 1, 467 (1963)

Type of Cancer: Peritoneal Cancer (Mesothelioma)

Method of Study: Correspondence - Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - asbestos worker

Material: Not Given

Location: England (New Castle)

Findings: One case of peritoneal mesothelioma in a case of asbestosis (autopsy)

Date: 1963

Reference:

Mancuso, TF and Coulter, EJ: Methodology in Industrial Health Studies: The Cohort Approach with Special Reference to an Asbestos Company, Arch Env Health, 6, 210 (1963)

Type of Cancer: Lung Cancer and Peritoneal Cancer

Method of Study: Epidemiological Study (Prospective)

Population Examined: 1495 employees of a manufacturer of asbestos products; employed anytime in 1938 or 1939 and followed from 1940 to mid 1960.

Nature of Exposure: Occupational - workers manufacturing asbestos products

Material: Not Given

Location: USA (Ohio)

Findings: Cancer of lung, bronchus, and trachea: 19 observed deaths, 5.6 expected deaths. Cancer of digestive organs and peritoneum: 18 observed deaths, 8.2 expected deaths (death certificates)

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Date: 1963

Reference:

Thompson, JG, Kaschula, ROC, and MacDonald, RR: Asbestos As A Modern Urban Hazard, S Afr Med J, 37, 77 (1963)

Type of Cancer: Pleural Cancer and Peritoneal Cancer (mesotheliomas)

Method of Study: Autopsy Survey

Population Examined: 500 consecutive autopsies (lungs) on subjects 15 years and over; performed at Groote Schuur Hospital

Nature of Exposure: Occupational and Environmental [assumptions]

Material: Not Given

Location: South Africa (Cape Town)

Findings: 132 cases (26.4%) showed asbestos bodies: 30% of males; 20% of females. Only 6% were thought to be of occupational origin.

Date: 1964

Reference:

Buchanan, WD: The Association of Certain Cancers with Asbestosis: International Congress of Occupational Health, 1963, Madrid, Excerpta Med Found, 2, 617 (1964)

Type of Cancer: Lung Cancer and Other Cancers

Method of Study: Autopsy Survey

Population Examined: 169 autopsy reports for 169 cases of asbestosis. Extension of earlier British studies; 1956 to 1962 [see Ann. Report for 1947, 1955]

Nature of Exposure: Occupational

Material: Not Given

Location: England (London)

Findings: Fifty cases of lung cancer, five cases of pleural mesothelioma in 135 male cases of asbestosis; 6 cases of lung cancer in 34 female cases of asbestosis (autopsy). Also, other cancers, number not specified for 1956 to 1962.

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Date: 1964

Reference:

Doll, R: Epidemiological Observations on Susceptibility to Cancer in Man with Special Reference to Age, Acta Un Intern Contra Cancr, 20, 747 (1964)

Type of Cancer: Lung Cancer

Method of Study: Epidemiological Study (Prospective)

Population Examined: One hundred and four men employed for more than 20 years

Nature of Exposure: Occupational

Material: Not Given

Location: England

Findings: Twenty cases of lung cancer were observed; two were expected (death certificates)

Date: 1964

Reference:

Elwood, PC and Cochrane, AL: A Follow-up Study of Workers from an Asbestos Factory, Brit J Ind Med, 21, 304 (1964)

Type of Cancer: Lung Cancer and Pleural Cancer (Mesothelioma)

Method of Study: Epidemiological Study (Prospective)

Population Examined: a) all persons who, since 1936, had worked in an asbestos works for a period of 6 months or longer (1153 men, 269 women), b) workers with 15 years or more exposure.

Nature of Exposure: Occupational - workers in an asbestos works

Material: Chrysotile

Location: South Wales

Findings:

a. One case pleural mesothelioma and 11 cases of lung cancer in 127 deaths with cause known.

b. Seven deaths due to lung cancer were observed, 3.02 were expected (death certificates).

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Date: 1964

Reference:

Entieknap, JB and Smither, WJ: Peritoneal Tumours in Asbestosis, Brit J Ind Med, 21, 20 (1964)

Type of Cancer: Cancer of Peritoneum

Method of Study: Case Reports

Population Examined: Autopsy Reports [one living case, also]

Nature of Exposure: Occupational - asbestos factory

Material: Chrysotile, crocidolite & amosite

Location: England (Essex)

Findings: 11 cases of abdominal tumours in association with exposure to asbestos - below average severity of asbestosis (ten by autopsy)

Date: 1964

Reference:

Fowler, PBS, Sloper, JC and Warner, EC: Exposure to Asbestos and Mesothelioma of the Pleura, Brit Med J, 2, 211 (1964)

Type of Cancer: Pleura Cancer (Mesothelioma)

Method of Study: Case Reports (2)

Population Examined: Autopsy Reports (3)

Nature of Exposure: Occupational: bag cleaner in asbestos factory and worker for a laundry - lagged pipes with asbestos and fitted presses with asbestos sheets

Material: Not Given

Location: England

Findings: Two cases of mesothelioma of the pleura without clinical signs of asbestosis. Both cases revealed asbestos bodies at autopsy.

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Date: 1964

Reference:

Hourihane D. O'B: The Pathology of Mesotheliomata and an Analysis of their Association with Asbestos Exposure, Thorax, 19, 268 (1964)

Type of Cancer: Pleural Cancer and Peritoneal Cancer (Mesotheliomas)

Method of Study: Autopsy Review

Population Examined: 34 cases of pleural and peritoneal mesothelioma (confirmed) from 1917 to 1962

Nature of Exposure: Not Given

Material: Unknown

Location: England (London)

Findings: 15 cases with asbestos bodies in lungs out of 30 cases of pleural or peritoneal mesotheliomas (where lung parts were available)

Date: 1964

Reference:

Navrátil M: Azbestoza, Plicni Rakovina A Tuberkoloza U Zamestnancu Zavodu Zpracujicich Azbest [Asbestosis, Lung Cancer and Tuberculosis in Employees of Asbestos Processing Plants], Prac Lek, 16, 345 (1964)

Type of Cancer: Lung Cancer

Method of Study: Epidemiological Study

Population Examined: 893 employees [observation period varied] workers in the dusty areas

Nature of Exposure: Occupational - workers in asbestos processing plants

Material: Not Given

Location: Czechoslovakia

Findings: Five cases of lung cancer in 39 cases of asbestosis, 3 cases of lung cancer with no asbestosis (X-ray)

Original Article: Czechoslovakian

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Date: 1964

Reference:

Oettle, AG: Cancer in Africa, Especially in Regions South of the Sahara, JNCI, 33, 383 (1964)

Type of Cancer: Lung Cancer and Pleura Cancer (Mesothelioma)

Method of Study: Epidemiological Study

Population Examined: Population in magisterial districts containing Cape asbestos fields compared to a control district of similar population and degree of urbanization. Also, population in districts adjoining the asbestos mining districts compared to similarly matched controls.

Nature of Exposure: Implied: occupational and environmental

Material: Crocidolite

Location: South Africa (Johannesburg)

Findings: Comparison of SMR's yield, a three fold increase in lung cancer in asbestos mining districts compared to controls and a lesser increase in lung cancer in adjoining districts compared to controls (death certificates)

Note: Adapted from Barnard Lecture, delivered April 21, 1962, at Washington University, St. Louis, MO.

Date: 1964

Reference:

Noeninckx, F: Asbestose et Cancers [Asbestosis and Cancer], Acta Tuberc Belg, 55, 102 (1964)

Type of Cancer: Lung Cancer, Pleural Cancer and Peritoneal Cancer (mesotheliomas)

Method of Study: Case Reports (3)

Population Examined: Ten cases of asbestosis (Autopsy Reports) (2))

Nature of Exposure: Occupational - workers in an asbestos factory

Material: Not Given

Location: Belgium

Findings: Three cases of lung cancer (one with an additional peritoneal tumor) in three cases of asbestosis (autopsy (2))

Original Article: French

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Date: 1964

Reference:

Owen, WG: Diffuse Mesothelioma and Exposure to Asbestos Dust in the Merseyside Area, Brit Med J, 2, 214 (1964)

Type of Cancer: Cancer of Pleura and Cancer of Peritoneum (Mesothelioma)

Method of Study: Case Reports

Population Examined: 16 cases of pleural mesothelioma, one case of peritoneal mesothelioma; 12 autopsies

Nature of Exposure: Occupational: 14 cases, Unknown: 3 cases

Material: Not Given

Location: England

Findings: 14 of 17 cases of pleural (peritoneal) mesothelioma known to be exposed to asbestos. Asbestos bodies were found in 7 out of 10 lungs examined. No clinical signs of asbestosis were present in these patients.

Date: 1964

Reference:

Selikoff, IJ, Churg, J, and Hammond, EC: Asbestos Exposure and Neoplasia, JAMA, 188, 22 (1964)

Type of Cancer: Lung Cancer, pleural and peritoneal mesothelioma, stomach, colon and rectum cancer

Method of Study: Epidemiological Study (historical - prospective)

Population Examined: Union records: 632 insulation workers who entered the trade before 1943 and were traced through 1962. (Minimum of 20 years since first exposure to asbestos)

Nature of Exposure: Occupational

Material: Not Given

Location: USA (New York metropolitan area)

Findings: Forty-five deaths due to cancer of lung or pleura compared to 6.6 deaths expected. Three of the pleural tumors were mesotheliomas; also one peritoneal mesothelioma. In addition were found twenty-nine deaths from cancer of the stomach, colon, or rectum, compared with 9.4 expected (death certificates)

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Date: 1964

Reference:

Smith, WE, Miller, L, Churg, J and Selikoff, IJ: Pleural Reaction and Mesothelioma in Hamsters Injected with Asbestos [Abstract], Proc Am Assoc Canc Res, 5, 59 (1964)

Type of Cancer: Pleural Cancer (Mesothelioma)

Method of Study: Experimental Study (animal)

Population Examined: 45 Golden Syrian hamsters

Nature of Exposure: Experimental: injections of 25 mg of asbestos in 0.5 cc, 0.9% NaCl.

Material: Amosite, harsh chrysotile, soft chrysotile

Location: USA (New Jersey)

Findings: One case pleural mesothelioma in 15 hamsters injected with amosite asbestos to date. Survivors are still being followed.

Date: 1965

Reference:

Anspach, M, Roitzsch, E, and Clausnitzer, W: Ein Beitrag zur Atiologie des Diffusen Malignen Pleura - Mesothelioms [Report on the Etiology of Diffuse Pleural Mesotheliomas], Arch Gewerbepath uGewerbehyg, 21, 392 (1965)

Type of Cancer: Cancer of Pleura (mesothelioma)

Method of Study: Case Review

Population Examined: 41 cases of pleural mesotheliomas observed between 1950 and 1964

Nature of Exposure: Occupational and Neighborhood
(1) Four asbestos weavers or spinners
(2) Two punchers of asbestos-containing material
(3) One puncher and winder of asbestos
(4) Two workers in production of asbestos tubes and ribbons
(5) Nine who lived or worked in vicinity of asbestos plant
(6) Seven with no asbestos exposure

Material: Not Given

Location: Germany (Dresden)

Findings: Of 41 cases of pleural mesotheliomas, 35 were thoroughly analyzed. In 18 cases an occupational or non-occupational exposure to asbestos was determined (autopsy)

Original Article: German

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Date: 1965

Reference:

Dutra, FR and Carney, JD: Asbestosis and Pulmonary Carcinoma, Arch Env Health, 10, 416 (1965)

[Editorial comment included]

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - pipe fitter

Material: Not Given

Location: USA (California)

Findings: One case of lung cancer in a case of asbestosis (autopsy)

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Date: 1965

Reference:

Elmes, PC, McCaughey, WTE and Wade, OL: Diffuse Mesothelioma of the Pleura and Asbestos, Brit Med J, 1, 350 (1965)

Type of Cancer: Pleura Cancer (Mesothelioma)

Method of Study: Epidemiological (Retrospective: case-control) lung sections by biopsy or autopsy.

Population Examined: lungs or lung sections from:

a. 42 patients with pleura mesothelioma and 42 control patients (no meso.)

b. 100 men without lung cancer (age 50-59)
100 men without lung cancer (age 60-69)
50 men with cancer of bronchus
50 controls matched to above

c. 20 lungs with asbestos bodies (with no cancer)
20 lungs (no cancer) without asbestos bodies

Nature of Exposure: Occupational

Material: Varied - Unknown

Location: Ireland (Belfast)

Findings:

a. 32 cases of pleura mesothelioma exposed to asbestos out of 42 vs. 11 out of 42 controls.

b. Asbestos bodies found in:
1. 14 out of 100 men (no cancer - age 50-59).
2. 27 out of 100 men (no cancer - age 60-69).
3. 9 out of 50 men (lung cancer) vs. 13 out of 50 controls.
4. 21 out of 24 cases pleural, mesothelioma vs. 6 out of 24 controls.

c. History of industrial exposure for 14 out of 20 patients with asbestos bodies vs. 5 out of 20 for controls.

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Date: 1965

Reference:

Jones-Williams, W: Asbestosis and Lung Cancer, Arch Env Health, 10, 44 (1965)

Type of Cancer: Lung Cancer

Method of Study: Review of Lung Parts

Population Examined: Lung parts and slides of 52 cases of asbestosis

Nature of Exposure: Occupational - fabricators, process workers and asbestos miners

Location: Wales

Findings: Ten cases of lung cancer in 52 cases of asbestosis (three of these cases were previously reported)

Date: 1965

Reference:

Selikoff, IJ, Churg, J and Hammond, EC: Relation Between Exposure to Asbestos and Mesothelioma, New Eng J Med, 272, 560 (1965)

Type of Cancer: Pleura Cancer and Peritoneal Cancer (Mesotheliomas); also lung cancer and stomach cancer

Method of Study:

1. Autopsy Survey
2. Lung (parts) Survey of Mesothelioma cases
3. Cause of Death Survey of Asbestos Insulation Workers

Population Examined:

1. 1500 consecutive autopsies (1953-1964)
2. 45 lung parts from mesothelioma cases
3. 307 consecutive deaths among asbestos insulation workers

Nature of Exposure:

1. Unknown
2. Unknown
3. Occupational - asbestos insulation workers

Material: Primarily chrysotile

Location: USA (New York)

Findings:

1. 4 pleural mesothelioma, 5 peritoneal mesothelioma, 7 bronchogenic carcinoma in 26 cases of asbestosis (autopsy)
2. Asbestos bodies in 12 lung sections out of 45 cases of mesothelioma
3. 4 cases of pleural mesothelioma, 6 cases of peritoneal mesothelioma, 53 cases of lung cancer and 34 cases of cancer of stomach or colon in 307 consecutive deaths among asbestos insulation workers

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Date: 1965

Reference:

Steel, SJ and Boyd, J: Pleural Calcification and Mesothelioma Following Exposure to Asbestos, Brit J Dis Chest, 59, 130 (1965)

Type of Cancer: Pleural Cancer (Mesothelioma)

Method of Study: Case Report

Population Examined: Biopsy Report

Nature of Exposure: Occupational (slight degree): in charge of the stores of a firm engaged in distributing a variety of asbestos insulating materials.

Material: Not Given

Location: England (London)

Findings: One case of pleural mesothelioma with asbestos bodies in biopsy specimen.

Date: 1965

Reference:

Smith, WE, Miller, L, Churg, J and Selikoff, IJ: Mesotheliomas in Hamsters Following Intrapleural Injection of Asbestos, J Mount Sinai Hospital (New York), 32, 1 (1965)

Type of Cancer: Pleural Cancer (Mesothelioma)

Method of Study: Experimental Study (animal)

Population Examined:

a. Fifteen male hamsters given a single right intrapleural injection of soft chrysotile.
b. Fifteen male hamsters similarly injected with harsh chrysotile.
c. Fifteen male hamsters similarly injected with amosite.
d. Fifteen male hamsters as controls.

Nature of Exposure: Experimental - right intrapleural injection of 25 mg of one of the asbestos preparations.

Material: Chrysotile and amosite

Location: USA (New Jersey)

Findings:

a. No tumors in 15 hamsters treated with soft chrysotile.
b. Two large pleural tumors in hamsters (15) treated with harsh chrysotile.
c. Two large pleural tumors and one small tumor found in hamsters (15) treated with amosite.
d. No tumors in control group.

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Date: 1963

Reference:

Knowles, LH: in "Case Records of the Massachusetts General Hospital," Edited by B. Castleman, New Eng J Med, 269, 747 (1963)

Type of Cancer: Pleural Mesothelioma

Method of Study: Case Report (1)

Population Examined: Autopsy Report (1)

Nature of Exposure: Occupational - installer of insulating material on pipes and boilers

Material: Not Given

Location: USA (Massachusetts)

Findings: One case of pleural mesothelioma in a case of asbestosis (autopsy)

Date: 1963

Reference:

Farina, S and Mazzanti, G: Asbestosi e Neoplasie Polmonari: Ulteriore Contributo au di Un Caso Clinico [Asbestosis and Lung Neoplasms: Further Contributions to a Clinical Case], Lavoro Umano, 15, 276 (1963)

Type of Cancer: Lung Cancer

Method of Study: Case Report (1)

Population Examined: X-ray Report (1)

Nature of Exposure: Occupational - insulator

Material: White asbestos

Location: Italy (Bologna)

Findings: One case of lung cancer in one case of asbestosis (X-ray)

Original Article: Italian

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