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172

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Asbestos Exposure and Neoplasia

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Building trades insulation workers have relatively light, intermittent, exposure to asbestos. Of 632 insulation workers, who entered the trade before 1943 and were traced through 1962, forty-five died of cancer of the lung or pleura, whereas only 6.6 such deaths were expected. Three of the pleural tumors were mesotheliomas; there was also one peritoneal mesothelioma. Four mesotheliomas in a total of 255 deaths is an exceedingly high incidence for such a rare tumor. In addition, an unexpectedly large number of men died of cancer of the stomach, colon, or rectum (29 compared with 9.4 expected). Other cancers were not increased; 20.5 were expected, 21 occurred. Twelve men died of asbestosis.

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ALTHOUGH PULMONARY CARCINOMA had been observed in the earliest studies of asbestosis, association between the two conditions was first suggested by Lynch and Smith in 1935.[1] Additional reports of such association followed. Perhaps the most striking data was presented in the annual report of the Chief Inspector of Factories of Great Britain for 1955.[2] Every death with asbestosis in the files of the Factory Department, from the first recognition of asbestosis as a disease entity, was studied. Altogether 365 such deaths were recorded (1924-1955). Sixty-five or 17.8% were found to be accompanied by cancer of the lung or pleura. Doll,[3] after reviewing the problem and adding data of his own, concluded that lung cancer was a specific industrial hazard of heavily exposed asbestos workers.

Nevertheless, some investigators have held that, while these observations might be suggestive, they did not establish an increased incidence of carcinoma of the lung in pulmonary asbestosis, and further, that the association was unproved.

The factor of selection was considered a potential weakness in evaluating reports of autopsy series. It was noted that complicated and unusual cases would be more likely to come to autopsy, thus raising the apparent frequency of associated lung neoplasms.[4] Further, it was argued that autopsy statistics, which dealt with particular groups of those who died, do not reflect total populations of asbestos workers.[5] Additional reservations were based on the frequent absence of data regarding exposure, smoking habits, and personal history, on the size of series, and on inadequate histological verification in some cases.

Within the last few years a number of additional problems connected with asbestos exposure have appeared, making clarification and resolution of the foregoing statistical uncertainty a matter of considerable concern. First, there has been greatly increased use of the various types of asbestos (a five-fold increase in world utilization of this group of minerals, from 500,000 tons to 2,500,000 tons per year in the last 30 years), as well as a greatly increased number and variety of industrial applications of asbestos (over 3,000 such uses now recorded). Second, suspicion has been growing that malignancy associated with asbestos exposure may include neoplasms other than carcinoma of the lung. Thus, a significant relationship has been claimed between diffuse mesothelioma of the pleura and peritoneum and asbestos exposure.[6]

This communication is concerned with investigations undertaken to study the following factors: (1) the incidence of deaths due to pulmonary carcinoma among a group of workers exposed to asbestos under United States industrial conditions in the past several decades, (2) whether or not such individuals would also be found to have an increased risk of other neoplasms, and (3) whether such risks would be present in an industry other than the asbestos-producing or asbestos-products industries, with which most reports in the past have been concerned but which would not necessarily represent the most important areas of asbestos exposure at this time. Further, it was hoped that study of an industry with asbestos exposure of limited extent and intensity would throw some light on the potential problems associated with minimal exposure to asbestos.

Materials and Methods

Our investigations have been concerned with 1,522 members of the Asbestos Workers Union in the New York metropolitan area, members of New York Local 12 and Newark, NJ, Local 32 of the International Association of Heat and Frost Insulators and Asbestos Workers. As the full title implies, these men are insulation workers. Although the union is considered one of the building-trades unions, its members do insulation work in a variety of industries, including shipbuilding. Called "laggers" in Great Britain, they are often designated "pipe coverers," "insulators," or "asbestos workers" in this country.

The union is one of the oldest in the country.

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The New York local, as the "Salamander Association of Boiler and Pipe Felters," was the first union of insulation workers in the United States. It amalgamated with other locals as the current Asbestos Workers Union in 1912. The stability of this union has been reflected in the stability of its membership rolls. "Once a pipecoverer, always a pipecoverer" has been of epidemiological importance to us and has made this group of men particularly suitable for the study of long-term effects of asbestos inhalation. Unlike unskilled workers exposed to asbestos inhalation in poorly paid industries, there is little labor turnover among insulation workers. Accurate employment records are maintained by the union, which has also been concerned with health problems in the industry.

The trade was badly hit during the depression; some men had to drop out and very few were added during the 1930's. By the end of 1942 the union rolls consisted mainly of men with considerable experience, plus a few who joined in 1940, 1941, and 1942. Between 1946 and 1962 union membership increased substantially.

Source of Data.—From union records, a list was prepared of every individual who was a member of either of the metropolitan locals on Dec 31, 1942, or who joined between that date and Dec 31, 1962. No one was omitted, whatever his subsequent work history. The 1942 list included 632 men; 890 men joined after 1942.

Personal data were obtained from union records, and the work history of each man was detailed, including withdrawal from employment (war service, other employment, retirement, illness). These data gave the baseline for calculation of the onset and duration of exposure. For members who had died, records of the Health and Welfare Fund provided date and place of death. Copies of death certificates were obtained on all but one of them. Autopsy protocols, histological specimens, and hospital records were obtained and reviewed in those deaths, approximately one half, in which the terminal illness had occurred in a hospital.

Statistical Analysis.—Previous studies have suggested that neoplasia associated with asbestosis seldom occurs until 20 years after first exposure to asbestos dust. Therefore, we decided to limit the present analysis to men with such an exposure history. Our complete records cover all members of the union (including active and retired members, both dead and alive) during the 20-year period from Jan 1, 1943, through Dec 31, 1962. However, with few exceptions, the only men with a history of 20 years or longer since first exposure to asbestos were the 632 men on the union rolls as of Jan 1, 1943. (The exceptions were a few men who joined the union after Jan 1, 1943, but who had been employed previously as asbestos workers elsewhere.) Of these 632 men, 255 died before Jan 1, 1963.

Table 1.—Man-Years of Experience of 632 Asbestos Workers Exposed to Asbestos Dust 20 Years or Longer

Age	Years 1943-1947	1948-1952	1953-1957	1958-1962
35-39	85.0	185.0	7.0	11.0
40-44	230.5	486.5	291.5	70.0
45-49	339.5	324.0	530.0	314.5
50-54	391.5	364.0	308.0	502.5
55-59	382.0	390.0	316.0	268.5
60-64	221.0	341.5	344.0	255.0
65-69	139.0	181.0	286.0	280.0
70-74	82.0	115.5	137.0	197.5
75-79	31.5	70.0	70.5	75.0
80-84	5.5	18.5	38.5	23.5
85+	3.5	2.0	8.0	13.5
Totals	1,912.0	2,478.0	2,336.5	2,011.0

Of these 632 men, 339 had been exposed to asbestos dust prior to 1924. In other words, as of Jan 1, 1943, 20 years or longer had elapsed since these 339 men were first exposed. The remaining 293 men reached the 20-years-since-first-exposure point at some time after Jan 1, 1943, and before the end of 1962. The 339 men who were first exposed prior to 1924 were counted in each of the 20 years (or up to the time of death of those who died). The 293 who were first exposed in 1924 or later were counted only after they reached the 20-years-since-first-exposure point (those who died being dropped at the time of death). When the statistics were completed, we found that we had records covering a total of 8,737.5 man-years of experience of men with a history of 20 years or longer since first exposure to asbestos dust.

Of the 8,737.5 man-years, 1912.0 were in the five-year period 1943-1947; 2,478.0 were in the period 1948-1952; 2,336.5 were in the period 1953-1957; and 2,011.0 were in the period 1958-1962. Table 1 shows the age distribution of the man-years in each of these five-year periods. Table 2 shows (1) the average age-specific death rates of all US white males during each of these periods, and (2) the average age-specific death rates from cancer of the lung, pleura, mediastinum, and trachea among US white males during each period, as reported by the US National Office of Vital Statistics.

The man-years were then multiplied by the corresponding reported US death rates to ascertain the *expected* number of deaths under the null hypothesis that the death rates of asbestos workers do not differ from death rates of all US white males (both age and date being taken into consideration). The results are summarized in Table 3.

Results

Total Deaths.—During the first five years (1943-1947) only 28 deaths occurred among the asbestos workers, whereas 39.7 deaths would have occurred had their age-specific death rates been the same as for all US white males during those years (Table 3). In other words, at the start of the study, the asbestos workers had below average death rates. This is by no means surprising. Indeed, such

Table 2.—Total Deaths and Deaths From Cancer of the Lung, Bronchus, Pleura, Mediastinum, and Trachea per 10,000 White Males per Year*

Age	1943-1947		1948-1952		1953-1957		1958-1962	
	Total	Lung Cancer†	Total	Lung Cancer†	Total	Lung Cancer†	Total	Lung Cancer†
35-39	36	....	30	....	26	....	25	1
40-44	55	1	48	1	43	1	42	1
45-49	85	2	78	3	72	3	70	3
50-54	133	4	124	5	115	6	116	7
55-59	196	5	189	8	178	10	173	11
60-64	295	7	281	10	276	14	272	17
65-69	435	7	417	11	416	17	418	21
70-74	634	6	605	11	586	16	607	21
75-79	977	6	915	10	878	14	866	17
80-84	1,453	5	1,353	8	1,346	12	1,363	15
85+	2,422	3	2,162	7	2,017	9	2,148	11

*Death rates as reported annually by the US National Office of Vital Statistics. A five-year average is given here for each period. Averag for 1958-1962 is a projection of 1958-1960, since 1961-1962 rates are not yet available.
†Death rates include cancer of the lung, bronchus, pleura, mediastinum, and trachea, assigned to international list code No. 47b-f pric to 1949 and to No. 160-164 thereafter.

is almost always found in the first few years of a prospective epidemiological study of this type. The explanation is almost certainly as follows: The 632 men in this analysis were actively employed as asbestos workers in 1942. Since disability from illness or other causes precludes employment in a trade of this type, these men were presumably well (or at least not disabled) at the start of the study period. Almost any group so selected as to exclude the ill and disabled has a lower death rate during the ensuing few years than does the general population, since ill and disabled persons have extremely high death rates. A selective effect of this type gradually wears off with time and largely disappears within five to ten years from the time of initial selection.

During the second five-year period (1948-1952) the death rate of the asbestos workers was slightly higher than the death rate of all US white males, ie, 54 observed deaths compared with 50.8 expected deaths. In later periods, the death rate of the asbestos workers was proportionately higher. For the period 1953-1957, there were 85 observed deaths compared with 56.6 expected deaths, and for the period 1958-1962, there were 88 observed deaths compared with only 54.4 expected deaths.

Table 3.—Observed and Expected Number of Deaths Among 632 Asbestos Workers Exposed to Asbestos Dust 20 Years or Longer

Cause of Death	Years 1943-1947	1948-1952	1953-1957	1958-1962	Total, 1943-1962
Total, all causes					
Observed (asbestos workers)	28	54	85	88	255
Expected (US white males)	39.7	50.8	56.6	54.4	203.5
Total cancer, all sites					
Observed (asbestos workers)	13	17	26	39	95
Expected (US white males)	5.7	8.1	13.0	9.7	36.5
Cancer of lung and pleura					
Observed (asbestos workers)	6	8	13	18	45
Expected (US white males)	0.8	1.4	2.0	2.4	6.6
Cancer of stomach, colon, and rectum					
Observed (asbestos workers)	4	4	7	14	29
Expected (US white males)	2.0	2.5	2.6	2.3	9.4
Cancer of all other sites combined					
Observed (asbestos workers)	3	5	6	7	21
Expected (US white males)	2.9	4.2	8.4	5.0	20.5
Asbestosis					
Observed (asbestos workers)	0	1	4	7	12

Cancer of the Lung, Pleura, and Trachea.—In each of the four five-year periods, far more deaths from cancer of the lung and pleura occurred among the asbestos workers than would have occurred had their death rates from these diseases been the same as for all US white males (Table 3). Altogether 45 of the 632 asbestos workers died of cancer of these sites, whereas only 6.6 such deaths would be expected from general US experience. Of these 45 deaths, 42 were recorded as due to bronchogenic carcinoma and 3 to neoplasms of the pleura. The pleural neoplasms were all recorded as mesotheliomas.

Thus it was found that the death rate from cancer of the bronchus and pleura was 6.8 times as high among these asbestos workers as in the general US white male population (both age and date being taken into consideration).

It may be asked whether the high rate of lung cancer among these asbestos workers could possibly be attributed to an unusually large proportion of cigarette smokers among them. We cannot answer this question directly, since we have not yet been able to ascertain the smoking habits of the men who died. However, the following pieces of evidence indicate that unusual smoking habits cannot account for the high death rate from lung cancer among these workers:

We have interviewed 320 of the 377 surviving members of the 1942 group. Table 4 gives a summary of the smoking habits in this group compared with a sample of men drawn from the general population of 1,121 counties in 25 states.[5] The union sample is somewhat inadequate since it does not include the men who died and does not include all of the present living members of the union. Nevertheless, it shows that a substantial proportion of asbestos workers never smoked cigarettes regularly. Certainly the 632 men in our analysis of death rates were not all heavy cigarette smokers.

In the general male population, lung-cancer death rates are about ten times as high among cigarette smokers as among nonsmokers; and the

Table 4.—Smoking Habits of 320 Asbestos Workers Exposed to Asbestos Dust 20 Years or Longer Compared With Sample of Men From the General Population*

Age	Never Smoked Regularly		Smoked Pipe, Cigar, Never Cigarettes		History of Cigarette Smoking	
	Asbestos Workers, %	General Population, %	Asbestos Workers, %	General Population, %	Asbestos Workers, %	General Population, %
45-49	9.3	18.8	4.6	7.5	86.1	73.7
50-59	14.3	19.9	6.1	9.9	79.6	70.2
60-69	20.3	23.6	10.1	16.2	69.7	60.2
70	25.5	37.1	11.8	23.9	62.7	39.0

*Sample of men from general population as reported by Hammond and Garfinkel.[7]

death rate from lung cancer increases greatly with the amount of cigarette smoking.[8] However, a large proportion of all men in the United States have a history of regular cigarette smoking. From data in a prospective study on smoking,[8] it may be estimated that if all men smoked a pack or more of cigarettes a day (ie, if all the nonsmokers, cigar smokers, pipe smokers, and light cigarette smokers had, instead, been heavy cigarette smokers) the lung-cancer death rate would be approximately 3.4 times as high as it is at this time.

From this we may conclude that even if *all* our asbestos workers had smoked a pack or more of cigarettes a day (and, indeed, from our sample we know they did not), and if exposure to asbestos were of no significance, then their lung cancer death rate would have been about 3.4 times as high as the rate in the general US male population. Clearly, the smoking habits of the asbestos workers cannot account for the fact that their lung-cancer death rate was 6.8 times as high as that of white males in the general population.

Gastrointestinal Cancer.—Rather to our surprise, the death rate from cancer of the stomach and the death rate from cancer of the colon and rectum were higher among the asbestos workers than would be expected from the rates reported for the US white male population, calculated in the same way as for lung cancer. Twelve deaths from gastric cancer occurred among the asbestos workers, as compared with only 4.3 expected. Seventeen deaths from cancer of the colon and rectum occurred among the asbestos workers, as compared with 5.2 expected.

Cancer of All Other Sites.—The combined death rate from cancer of all sites other than lung and pleura, and stomach, colon, and rectum was not increased. Twenty-one such deaths occurred among asbestos workers, as compared with 20.5 expected.

Asbestosis.—Of the 255 deaths, 12 were due to asbestosis (pulmonary insufficiency, cor pulmonale). The lapsed time from first asbestos exposure to death from asbestosis averaged 45.8 years, with a range of 32 to 59 years.

Comment

Carcinoma of the Lung.—The results with regard to carcinoma of the lung are clear. Industrial exposure to asbestos by insulation workers, as studied here, results in a marked increase in the incidence of cancer of the lung, approximately six to seven times the expected incidence. Altogether, 45 (17.6%) of 255 men with more than 20 years elapsed since the onset of exposure died of cancer of the lung or pleura.

These data do not give the "incidence of cancer of the lung in asbestosis." They relate to the specific conditions of our investigation: to a group of men with only intermittent exposure to materials containing limited amounts (often 2% to 20%) of asbestos under working conditions varying from very dusty, as in extracting old insulation in closed quarters, to those with little dust exposure, as in building construction in open air. Moreover, they relate to the relatively recent past, in a trade with the shorter work week of the strong building trades unions, in an era when industry has been aware of potential asbestos hazard and the working population has had some consciousness of potential risk associated with dust exposure. These data would not necessarily apply to asbestos exposure in other industries, such as the factory production of asbestos products, the asbestos textile industry, etc, where conditions of employment might be quite different. Our results do not contradict the even higher incidence of lung cancer suggested in other studies [3]; they are merely a shade less striking.

Diffuse Pleural and Peritoneal Malignancy—Mesothelioma.—Determining the incidence of diffuse pleural mesothelioma is complicated by the insecurity of its histological verification. While some pathologists will so categorize a high proportion of diffuse pleural tumors, in the experience of others it is a very rare tumor and may be mimicked by anaplastic peripheral carcinoma of the lung and diffuse fibrosarcoma of the pleura. It is difficult to evaluate completely the published reports of diffuse pleural mesothelioma in asbestosis in the absence of complete details of each case.

To the present time, there has been no information concerning the *incidence* of diffuse pleural mesothelioma in asbestosis, since the published cases are reported without reference to a total population in which they occur. Nevertheless, the

growing number of reports of individual cases suggests that these tumors are perhaps becoming relatively frequent complications of asbestos exposure.

Our observations in this series are similarly suggestive. In three of the 255 deaths among the men who had worked for 20 years or more, the examining pathologist considered the death due to diffuse pleural mesothelioma, and in the two cases in which we have been able to review the histological material, the histological appearance was that often so categorized, and asbestos bodies were present. This incidence of more than 1% of deaths from pleural mesothelioma is strikingly high for a tumor which is generally considered to be extremely rare. In one case in our series pathological examination suggested diffuse peritoneal mesothelioma. This single experience is too fragmentary for evaluation.

Gastrointestinal Carcinoma.—Isolated instances of gastrointestinal carcinoma in the presence of asbestosis have been known, but there have been no data to indicate that these were more than coincidental findings. Among the asbestos workers studied here, cancer of the stomach, colon, and rectum was three times as frequent as expected. These data suggest that there may perhaps be an etiological relationship between industrial asbestos exposure and carcinoma of the gastrointestinal tract.

Environmental Asbestos Exposure.—The recent demonstration, by South African [6] and British [9] investigators of pleural and peritoneal neoplasms among individuals who had chance environmental exposure to asbestos many years before raises the very important question of possible widespread carcinogenic air pollution. The possibility of environmental exposure has long been known. Soon after the initial clarification of asbestosis as a clinic entity, Haddow [10] demonstrated asbestos bodies in a man not employed in the industry but living next door to an asbestos factory. This finding was later mirrored in the finding of chronic beryllium disease among residents of a community near a beryllium factory.[11] What is new, however, is an appreciation of the potential extent of the problem. Thomson and associates [12] have reported the frequent findings of asbestos bodies in the lungs of urban dwellers. Among 6,312 individuals x-rayed in an area about an asbestos mine in Finland, Kiviluoto [13] found 499 cases of pleural calcification of the type characteristically seen among asbestos workers, without obvious cause. In a comparable area without any asbestos mine, no cases were found among 7,101 persons x-rayed. It should be noted that these were not people who worked in the mine—none did—but, rather, were farmers, housewives, and others who lived in the general location. In one subject who came to autopsy, polarized-light microscopy demonstrated asbestos fibers in the lung. Similarly, the lung of a cow grazing near the mine also showed the presence of asbestos.

A particular variety of environmental exposure may be of even greater concern. Asbestos exposure in industry will not be limited to the particular craft that utilizes the material. The floating fibers do not respect job classifications. Thus, for example, insulation workers undoubtedly share their exposure with their workmates in other trades: intimate contact with asbestos is possible for electricians, plumbers, sheet-metal workers, steamfitters, laborers, carpenters, boiler makers, and foremen; perhaps even the supervising architect should be included.

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