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Malignancies in Asbestos Workers

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WITHIN recent years and months a considerable amount of evidence has appeared in the literature which indicates that asbestosis is directly related to the incidence of malignant tumors and cancer.¹⁻³

As early as ten years ago a Pennsylvania pathologist reported that he had seen at autopsies many cancer cases in persons who also suffered from asbestosis. The pathologist is on the staff of a hospital which receives most of the patients from a nearby town where a large asbestos producing plant is located. The findings of the pathologist have created concern in the asbestos industry and it was felt appropriate for the Pennsylvania Health Department to review the problem.

Exposures in the Plant

The following information was obtained from the files of the health department which has studied environmental exposures of workers in this plant on several occasions in the past 30 years. During this time there has been a tremendous improvement in dust conditions in all operations and dustiness has been held close to or below the present threshold limit.

The textile department used chrysotile, primarily, for many years. It was not uncommon for the milled fiber received by the textile plants to contain 30% or more of fines. The fiber of today is very much cleaner than that received prior to 1950. The use of light oil in the blending department began around 1955. This was helpful in improving conditions and minimizing dust. Prior to 1950 amosite was processed in small quantities for making thermal blankets. Although the processing of amosite never exceeded one card and the operations were at times intermittent, this operation was much dustier than from cards processing chrysotile. Crocidolite has never been handled in the textile department.

In the friction products operations extensive changes in the formulations have

taken place over the past 30 years. Prior to 1945, coal tars and pitches were commonly used as impregnants in making brake linings, clutch facings, and packing materials. Since 1945, these have been essentially replaced by resins and other materials so that at present only a very small amount of tar and pitch is used in packing materials. A small amount of crocidolite is still used in making some packings.

The Study

Since asbestosis is a disease which, once established, progresses even after exposure to dust ceases, it was decided not to ask plant management for cases known to them. Instead, the record rooms of six hospitals which draw their patients from the area of the asbestos plant were checked for cases of asbestosis. Admissions only for the period between 1956 and 1964 were included. Seventy-five hospital records coded as asbestosis were located. Asbestosis was diagnosed in these people on admission, by x-ray, or at autopsy, or asbestosis was mentioned in the differential diagnosis.

After obtaining the 75 records, medical, occupational, and smoking histories were obtained for all these former patients. Many were deceased and their survivors had to be contacted. Other data were obtained from plant management. Seven either had not worked at the asbestos plant under study or the diagnosis had been changed. This left 68 asbestos workers who had worked at one time in the above-mentioned textile and friction materials plant. Further study of the records showed that 21 of these not only had evidence of asbestosis but also had suffered from malignancy. By the time of the

TABLE 1.—Number of Cases and Duration of Occupational Asbestos Exposure by Departments

Exposure Duration	Department			
	Textile	Friction	Textile and Friction	Unknown
Less than 10 years	1	0	1	1
10-20 years	3	3		
20-30 years	3	1	1	
30+ years	6		1	

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TABLE 2.—Summary of Cases Studied

Case	Birth	Death	Type of Tumor	Length of Employment in Asbestos	Type of Employment	Smoking	Remarks
1	1911	1962	Bronchogenic carcinoma, histologic type unspecified	1935-1957	Yarn twisting 1934-1962	12-15 cigarettes	
2	1906	1959	Squamous cell bronchogenic carcinoma	1929-1959	Weaver 1929-1959	1 pack/day	
3	1898	1958	Squamous cell bronchogenic carcinoma	1918-1928	Breakline weaver 1918-1928	No cigarettes	30 yr foundry work
4	1907	1961	Oat cell bronchogenic carcinoma	1927-1957	Weaving and later loom fixer	No cigarettes	
5	1895	1961	Squamous cell bronchogenic carcinoma	1947-1961	Laborer sweeper, picker house	1 pack +/day	Also cirrhosis of liver
6	1901	1956	Bronchogenic adenocarcinoma	Only 6 mo 1919	Weaver—later lath foundry worker	Cigars only	Probably not due to asbestos
7	1901	1957	Anaplastic bronchogenic carcinoma	3 mo only in 1923	Area unknown, later hotel operator 1923-1957 Linotype operator 1921-1923	No cigarettes	Probably not asbestos
8	1895	1958	Bronchogenic carcinoma, histologic type unspecified	1925-1937	Carding room, gardening for 19 yr thereafter	1 pack/day	
9	1897	1958	Squamous cell bronchogenic carcinoma	1922-1954	Weaver 1922-1954	Less than 10 cigarettes/day	
10	1905	1961	Alveolar cell carcinoma of the lung	1950-1960	Friction materials, laborer on lathe	Unknown	
11	1895	1960	Carcinoma of the lung, origin and type unknown	1926-1960	Inside driver in weaving room	No cigarettes	Diagnosis from hospital records no autopsy
12	1903	1958	Lung tumor, x-ray diagnosis	1919-1955	Loom fixer, machine shop foreman, toolmaker	2-3 cigarettes/day	
13	1907	1961	Anaplastic bronchogenic carcinoma	1928-1961	General foreman—spinning before last job	No	
14	1901	1961	Intra-abdominal adenocarcinoma, origin unknown	1934-1942	Most of the time in friction products, spinning 1922-1937, later upholsterer	1 pack/day	
15	1894	1956	Carcinoma of the colon	1922-1956	Weaver	5-10 cigarettes/day	
16	1884	1959	Lymphatic leukemia, chronicity unknown	6 mo only 1941	Sweeper and laborer June 12, 1941 Mechanics helper for 45 years for trucking company	No	Probably not due to asbestos
17	1901	1962	Malignant lymphoma	1926-1942	Carding room supervisor	No cigarettes, little pipe	
18	1888	1964	Chronic lymphatic leukemia	1938-1947	Laborer—handtrucker—supplied weavers with spools; farmer till 1937, sexton at church till death	Very few cigars only	3 coronaries
19	1877	1960	Acute leukemia, type unknown Carcinoma of throat, origin and type unknown	1922-1949	Shipping room only	5-10 cigarettes/day	? asbestosis
20	1895	1958	Multiple myeloma Carcinoma of prostate, metastatic	1935-1957	Weaver—loom fixer, textile foreman 1935-1947, packing mill 1947-1957	Pipe only	
21	1894	1957	Carcinoma of bladder	1917-1937	Supervisor friction mill 20 years 1917-1937, ice cream maker 20 years 1937-1957	1 pack +/day	

study all 21 had died. Ten of these cases have also been reported by O'Donnell in a paper which appeared in *Cancer* in August 1966.⁴ Thirteen of these had lung cancer

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and eight had various other growths which included two abdominal cancers, one bladder cancer, two lymphatic leukemias, one acute leukemia, one lymphoblastoma, and one multiple myeloma. No cases of mesothelioma were in this group. There were four cases in former plant employees but these employees had been admitted to hospitals either prior to 1956 or after 1964 and because of that are not included in this study.

The diagnosis of the condition of these 21 patients had been established in 13 by autopsy, in four by operation, in two by biopsy, and in two by x-ray only.

The death certificates of all 21 were obtained. The malignancy diagnosis was reported on 15 death certificates. Six were signed out as follows: two as cardiac failure, one as coronary disease, and three as asbestosis. If death certificates alone had been utilized in this study, these six cases of malignancy would have been missed.

The smoking history of the 13 lung cancer patients revealed that five had never smoked, seven smoked, and in one case no smoking history was obtainable. Of the eight patients with other malignancies, three were cigarette smokers, two never smoked, and three were cigar smokers only.

Of the 21 patients with cancer, 13 had worked in the textile department of the plant only, for a sum total of 301 years. Four worked in the friction materials department for a total of 48 years. The department where one man had worked remains unknown and three others worked at various jobs which included both textiles and friction materials (Table 1).

Two of the 13 lung cancer and one of the lymphoblastoma patients had worked in the asbestos plant for a period of less than six months each, which is a rather short exposure. One wonders if this short exposure could have contributed towards their disease. Eighteen of these 21 patients had started work in the plant prior to 1940 and 12 had started work prior to 1920. Of the 21 patients with cancer 9 were between 50 and 60 and 12 were over 60 years of age (Table 2).

Comments and Conclusions

The incidence of malignancy in this selected group of hospital admissions with asbestosis was very high—21 out of 68. This is eight times higher than in the general

population 45 years of age and over, for the eight years of the study period.⁵

The incidence of 19% (or 16% if we do not consider exposures of less than one year) of lung cancer in this group of workers with asbestosis is comparable to that reported by Isselbacher¹ who summarized data of various authors and reported that of 603 persons with asbestosis, lung cancer was found in 83 (13.8%). It is also close to that reported in the literature review by Behrens⁶ who collected 44 cases of lung cancer (14%) in 309 patients with asbestosis.

Only three patients with these malignancies had their first exposure after 1940, when dust conditions had been much improved. A repeat study in the future may clarify whether this reduction of cancer occurrence in more recent employees is due to a latent period, to the age factor, or to the dust control measures instituted by the plant.

The patients with lung cancer were generally younger than those with cancers of other organs. Eight of those in the lung cancer group were under 60 and all eight of those in the other group were over 60 (Table 2).

Summary

A study of 68 hospital admissions with asbestosis from an asbestos textile and friction materials plant included 21 malignancies—13 of these were carcinoma of the lung and eight carcinomas of other organs. Eighteen of the patients had exposures to asbestos in their occupational environment for a period of 10 to 36 years. Only three patients had their first exposure after 1940.

Extensive dust control measures have been instituted by the plant.

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Mesothelioma and Asbestos Exposure

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WITHIN the past five years several arti-
cles have called attention to the association
between mesotheliomas of the pleura and
peritoneum with asbestos exposure.¹⁻³

Wagner et al⁴ studied 33 cases of meso-
thelioma. All but one had probable exposure
to crocidolite, the blue asbestos.

Asbestos has become a ubiquitous materi-
al in our civilization. Cauna et al⁵ reported
that asbestos bodies were found in the lung
smears of 41% of 100 consecutive autopsies
at the Presbyterian University Hospital in
Pittsburgh. Similar findings were reported
by Thompson^{6,7} in 500 consecutive lung
smears from Capetown, South Africa, and
Miami, Fla. Asbestos bodies were found in
30% of the men and 20% of the women. As-
bestos has been conclusively associated with
increased incidence of lung cancer and other
malignancies^{8,9} and an increasing number
of studies associate its presence with malig-
nant mesothelioma of the pleura and perito-
neum.

Pathology

Mesotheliomas of the pleura and perito-
neum are rare neoplasms. Controversy in-
volves histological types, nomenclature, ori-
gin, and their very existence. Recently,
mesotheliomas as an entity have become
generally accepted. Their morphologic vari-
ability makes classification difficult and dif-
ferentiation from other malignancies is often
a problem.

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17120 (Dr. Lieben).

Sacconi and Coblenz¹⁰ give the incidence
of pleural mesotheliomas as 1.1 cases per
1,000 autopsies. Campbell reported four
cases of pleural mesotheliomas in 3,533 con-
secutive autopsies.¹¹

Mesothelioma occurs primarily in adults
and is twice as common in males as in fe-
males.^{10,12}

Pleural mesotheliomas occur equally on
the right and left though Weissman feels
that pleural mesothelioma occurs on the
right more frequently than on the left
side.¹²

The criteria for diagnosis of pleural meso-
thelioma are presence of a firm pleural mass
encasing the lung, histological structure
compatible with mesothelioma, and absence
of a demonstrable primary malignant neo-
plasm elsewhere. The histologic architecture
may be mesenchymal, "epithelial," or
mixed.

A complete autopsy is necessary for une-
quivocal diagnosis, but for the purpose of
this study, criteria were made less rigid in
that unautopsied cases were accepted if a
definite diagnosis of pleural mesothelioma
had been made by biopsy, and malignancy
elsewhere had been excluded clinically;
chest x-ray examination, bronchoscopy, and
cytologic studies of sputum or bronchial
washing assisted in excluding the presence
of bronchial carcinoma.

Primary tumors of the peritoneum are
among the rarest of tumors. Generally called
mesotheliomas, they form large spreading
masses over the peritoneum and histologi-
cally appear the same as pleural mesothe-
liomas. As with pleural mesotheliomas, ex-
clusion of a primary tumor is necessary.

This study is an attempt to learn the ex-
tent of the relationship of asbestos exposure
with mesothelioma diagnosed in southeast-
ern Pennsylvania.

Method

One hundred and sixty-two hospitals serving a population of 6½ million people were requested to report all mesotheliomas diagnosed between 1958 and 1963. Replies were received from 152 hospitals. Hospital records of 62 reported cases were reviewed and only mesotheliomas confirmed by operation, biopsy, or autopsy were included in the study. Forty-two cases satisfied our criteria. There were 34 mesotheliomas of the pleura and eight of the peritoneum. Among the pleural mesotheliomas there was a definite preponderance for occurrence on the right side of the chest. Of 34 pleural mesotheliomas only seven occurred on the left side, 25 on the right side, and two were not stated.

Sections of as many of the tumors and lungs as possible were borrowed and reviewed by a single consultant pathologist familiar with mesotheliomas. In the 15 instances in which lung sections were available, they were examined for the presence of asbestos bodies. All slides were reviewed without the benefit of the complete history and autopsy protocol available to the pathologists who made the original diagnosis.

Results of the 33 cases reviewed (Table) by our pathologist agreed with those of the outside pathologists in 17 cases; he rejected seven cases as unacceptable histologically, had serious doubts in nine cases (of these one slide was read as metastasis and one slide as anaplastic malignancy). Of the 15 cases in which lung tissue was available, asbestos bodies were identified in seven.

The discrepancies between the original pathological diagnosis and that of our pathologist are reported to illustrate the difficulties and disagreements which are so frequent in the diagnosis of this tumor. For inclusion in this study the diagnoses of the originally reporting pathologists have been accepted and cases reported by them were investigated.

Efforts were made to obtain a complete employment and residence history for each patient. Inquiry was also made into the employment history of family contacts. Data were obtained from the individual if alive, from family members, or employers.

Of the 42 patients, ten had definite occupational exposure to asbestos during lifetime, three were family contacts of asbestos workers, eight either lived in the immediate neighborhood of asbestos plants or had been employed next to an asbestos plant. Ten patients had a questionable asbestos exposure and, in the other 11 patients, either no asbestos exposure could be elicited on direct questioning or no survivor could be located.

Table 1.—Readings of Consultant Pathologist

Case No.	Mesothelioma	Asbestos Bodies
1-0	Yes	No lung tissue
3-0	Not acceptable	Yes
4-0	Probably not	No lung tissue
5-0	Yes	Yes
6-0	Probably not	Yes
9-0	Probably not	No lung tissue
10-0	Yes	Yes
2-N	Yes	No lung tissue
3-N	Probably not	No lung tissue
4-N	Not acceptable	No lung tissue
6-N	Yes	No lung tissue
1-F	Yes	No lung tissue
2-F	Yes	No lung tissue
3-F	Yes	No lung tissue
1-Q	Probably not	No lung tissue
2-Q	Yes	Yes
4-Q	Yes	No
5-Q	Probably yes	No
6-Q	Not acceptable	No
7-Q	Yes	No lung tissue
8-Q	Yes	No
9-Q	Probably not	No
10-Q	May be Metast	No
1-X	Yes	Yes
2-X	Yes	No lung tissue
3-X	Not acceptable	No lung tissue
4-X	Not acceptable	No lung tissue
5-X	Anaplastic malignancy	No
6-X	Probably not	No
7-X	No epithelial cells	No lung tissue
	Mesothelioma must be proven	
8-X	Probably not	No lung tissue
9-X	Yes	No lung tissue
10-X	Yes	Yes

Exposure of Ten Mesothelioma Patients Who Worked With Asbestos.—Patient 1-0 worked 35 years in the textile department of a large asbestos plant.

Patients 2-0, 3-0, and 4-0 worked more than 20 years in asbestos insulation plants and patient 5-0 worked in an insulation plant for only one year.

Patient 6-0 worked 15 years in a plant manufacturing acoustic tile and linoleum.

Patient 7-0 was a boiler maker in a railroad yard where, for 25 years, he worked on insulation of steam engines.

Patient 8-0 built bakery ovens in which large amounts of asbestos insulation were used.

Patient 9-0 was a certified accountant who worked more than 30 years in the office of an asbestos textile plant.

Patient 10-0 was a plasterer who came in contact with a large amount of asbestos in his work.

Of these ten men, patients 1-0, 8-0, and 10-0 had mesotheliomas of the peritoneum; the other seven men had pleural mesotheliomas.

Neighborhood Cases.—Patient 1-N was a 55-year-old woman who never had any occupa-

ional asbestos exposure. Her work was always secretarial; she was born and lived until the age of 8, in the immediate neighborhood of an asbestos textile and friction material plant where patient 1-0 had worked for 35 years. From the age of 18 she lived for 30 years across the street from the plant where patient 6-0 had worked for 15 years.

Patient 2-N, a clergyman from 1935 until his death in 1961, never had any occupational asbestos exposure. Prior to becoming a minister he lived for 19 years within one half of a mile of the insulation plant where patients 3-0, 4-0, and 5-0 had worked as insulation manufacturing workers.

Patient 3-N never had any occupational asbestos exposure except that, 20 years prior to his death, he had worked for one year across the street from the insulation plant mentioned in the history of patient 2-N.

Patient 4-N worked for 26 years across the street from the insulation plant mentioned in connection with patients 2-N and 3-N.

Patients 5-N, a nurse, and 6-N, a meat distributor, had no occupational exposure nor family contact with asbestos. They both lived within three fourths of a mile of two asbestos plants in a town with the greatest incidence of mesotheliomas in this study.

Patients 7-N and 8-N were both foremen in a storage battery plant. A careful check of the plant and their employment records revealed no asbestos exposure, past nor present. The plant is located less than 1½ miles from an asbestos textile plant. The exposure of these two cases is questionable.

Patients 1-N and 4-N had peritoneal and patients 2-N, 3-N, 5-N, 6-N, 7-N, and 8-N had pleural mesotheliomas.

Mesothelioma Patients With Family Contacts Exposed to Asbestos.—Patient 1-F, a 3-year-old child, was the daughter of a ceramic engineer who worked in an insulation plant that utilizes 400 tons of Canadian chrysotile and 1,500 tons of South African amesite annually.

Patient 2-F, a 40-year-old nurse, never had any occupational asbestos exposure, but her father had worked for 35 years in the insulation plant where patients 3-0, 4-0, and 5-0 had worked and which was also credited with three neighborhood cases. The nurse's brother also had worked in this plant for one year.

Patient 3-F, a 67-year-old woman, never had any asbestos exposure nor had she lived near an asbestos plant. She had two sons who worked as insulators in a shipyard for six years. These sons lived at home until 15 years prior to their mother's death.

Patients 1-F and 3-F had peritoneal and patient 2-F pleural mesotheliomas.

Mesothelioma Patients With Questionable Asbestos Exposure.—A study of these ten men elicited either a relatively minor or questionable exposure to asbestos.

Patient 1-Q was a welder for 35 years. According to a common reference,¹³ eight out of 12 welding electrodes contain asbestos, which is used as a filler.

Patient 2-Q was a self-employed Swiss-born Swiss cheesemaker. A thorough study of the processes of Swiss cheese manufacture revealed no use of asbestos. During the study of the manufacturing process a 500-gal boiler was noticed. This boiler was covered with a friable asbestos insulation which flaked off on contact.

Patient 3-Q, a 14-year-old boy with mesothelioma, had no occupational contact with asbestos nor did any of his family. On questioning, the boy's father told the authors that his boy had lived with him and had helped him while he had replaced most of the plaster board during extensive remodeling of his house. Plaster board contains a high percentage of asbestos.

Patient 4-Q is employed in industrial sales and never had any occupational asbestos exposure. Extensive questioning revealed that, on two occasions several years before, he applied asbestos insulation to boilers in his home, mixing asbestos cement himself. His total exposure during these applications was only a matter of hours.

Patient 5-Q was a brewery worker for 20 years. The brewery was no longer in business when the case was investigated. Reviewing the literature of beer production the following paragraph was discovered:

"When ready for packaging the beer is filtered through pulp filters consisting essentially of cotton fibers and asbestos. After each filtration this 'FILTERMASS' is removed, mangled, and washed in clear, warm water, then bleached and sterilized at 160 to 180 F with chlorine. The washed pulp then goes directly to a pad-forming machine where it is compressed at 89 to 90 pounds per square inch to form new filter pads.¹⁴"

Asbestos-containing pipe insulation is used in breweries.

Patients 6-Q, 7-Q, and 8-Q were all steel workers. Patient 6-Q was a crane operator; 7-Q a forger; and 8-Q a foreman and supervisor. In all cases the companies did not recall any asbestos exposure for these men. Pipe insulation containing asbestos is extensively utilized by steel companies.

Patient 9-Q was a spinner in a silk company

from 1925 to 1938, and later in a plastic fabrication plant which utilized fiber glass; he also had been a welder for 25 years. He thinks he has used asbestos but could not recall when and where.

Patient 10-Q, a 63-year-old man, was a core-maker all his life. He worked in two foundries in one of which asbestos cement is used in small quantities but, according to the plant manager, the core-maker did not have any contact with this material. The son stated that his father had used asbestos pipe insulation for pipes in the basement of their home several years prior to the onset of his illness and that he had done some sawing of this pipe insulation material.

All cases in this group had pleural mesotheliomas.

Mesothelioma Patients Without Asbestos Exposure.—In the other 11 patients (1-X to 11-X) no occupational, familial or neighborhood asbestos exposure evidence could be elicited. Ten of these patients had mesothelioma of the pleura and one peritoneal mesothelioma.

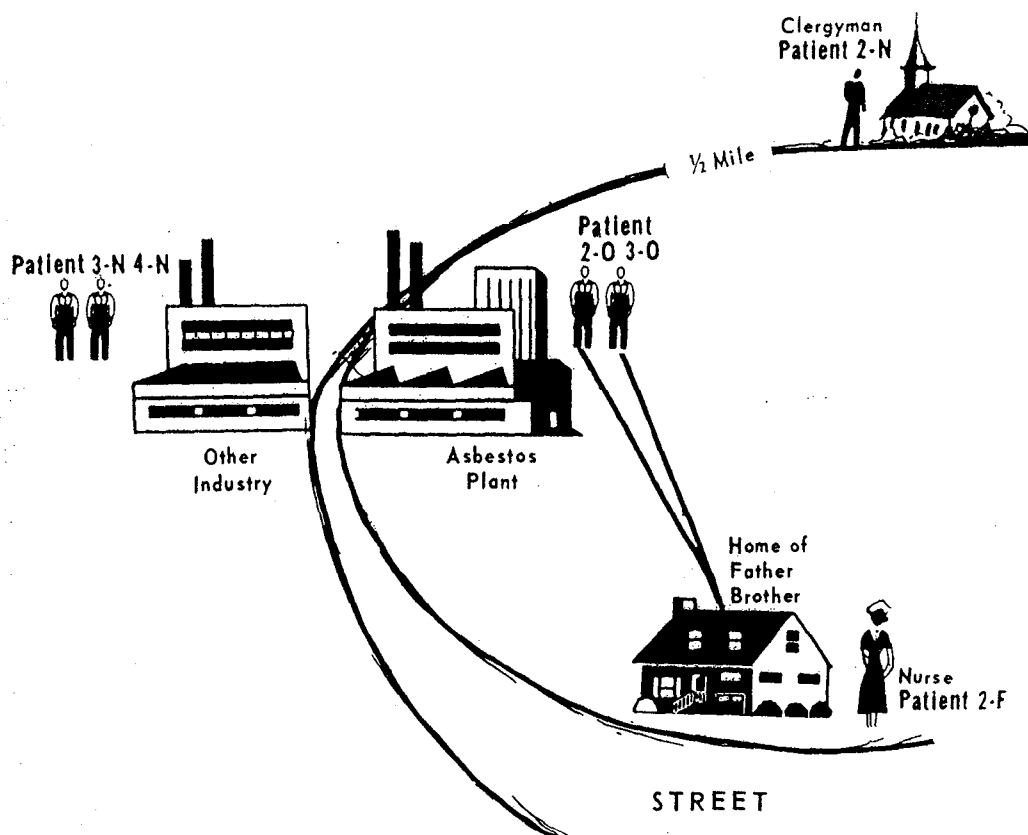
Comment

This study presents a good deal of circumstantial evidence and many unanswered questions.

Asbestos is a ubiquitous material used much more frequently than is generally realized. Some uses, such as in the brewery, were not previously known to the writers. There are undoubtedly many others.

If we assume that asbestos may be the causative or trigger agent for malignant mesothelioma in some of the cases described above, we must admit that the minimal dose-effect relationship and duration of a latent period are unknown. The occupational exposure of the insulation workers or asbestos textile workers were certainly many thousand times higher than those of the neighborhood cases or family contacts. Similar findings have recently been reported from England.¹

The attack rate for mesotheliomas is ex-



Occupational, neighborhood, and family contact patients with mesothelioma associated with one insulation plant.

Content

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Nurse
Patient 2-F

tremely low. Not all mesotheliomas were re-
ported to us by the hospitals, but, even if we
double the incidence, only a minute fraction
of the exposed population was affected.
There are precedents for this with beryllium
disease which acts in a somewhat similar
pattern; occupational diseases, familial con-
tacts, neighborhood cases plus a very low
attack rate, and a long latent period be-
tween exposure and onset of disease.

Another question which arises is why
pleural mesotheliomas are so much more
frequent than peritoneal mesotheliomas.

The most striking finding of this study
was that of the 42 mesotheliomas which
came from a geographical area of approxi-
mately 30,000 sq mi, six were clustered in
and around an insulation plant (Figure).
These included two insulation manufactur-
ing workers (Cases 2-0 and 3-0), three
neighborhood cases (Cases 2-N, 3-N, and 4-
N) and one family contact (Case 2-F)—the
daughter of an insulation worker.

Summary

Forty-two cases of mesotheliomas report-
ed from 152 hospitals over a five-year peri-
od, were studied with regard to exposure to
asbestos. Survivors or employers, or both,
were questioned regarding the possibility of
asbestos exposure. Ten patients actually
worked in asbestos plants; eight lived or
worked close to an asbestos industry; three
patients were family members of asbestos
workers. In ten patients a history of as-
sumed exposure to asbestos was obtained
after prolonged questioning. In 11 other pa-

tients no history of asbestos exposure could
be obtained.

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DISCOVERY OF QUININE

Many of the drug sources known in ancient times were apparently discovered by accident. For example, according to an old South American Indian legend, the curative power of cinchona bark (containing quinine) for malaria was discovered by a sick, feverish Indian lost in the jungle. He quenched his thirst by drinking from a pool of water. From the bitter taste of the water, he recognized that it was tainted with the poison from the quina-quina tree. Although he shared this fictitious belief, he drank deeply so as to bring about a quick death. To his great surprise, he recovered completely. When he returned to his village, he told the store of his cure and thereafter cinchona bark was used as a medicine for the fever prevalent in that region. The Incas later taught the Spanish conquistadors that malaria could be cured with cinchona extract.—Rossman, R.E.: The History and Significance of Serendipity in Medical Discovery, *Trans Coll Physicians Phila* 33:104-120 (Oct) 1965.