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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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From the Division of Occupational Health, De-
partment of Health, Harrisburg, Pa.

Read before the Ninth International Cancer Con-
gress, Tokyo, October 1966.

Reprint requests to PO Box 80, Harrisburg, Pa
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	No lung tissue
4-Q	Yes	Yes
5-Q	Probably yes	No
6-Q	Not acceptable	No
7-Q	Yes	No
8-Q	Yes	No lung tissue
9-Q	Probably not	No
10-Q	May be Metast	No
1-X	Yes	No
2-X	Yes	Yes
3-X	Not acceptable	No lung tissue
4-X	Not acceptable	No lung tissue
5-X	Anaplastic malignancy	No lung tissue
6-X	Probably not	No
7-X	No epithelial cells	No
	Mesothelioma must be proven	No lung tissue
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-

Insulant Pathologist

Asbestos
Bodies

No lung tissue
Yes
No lung tissue
Yes
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No lung tissue
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No lung tissue
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amounts were used.

an accountant who
worked in the office of an

worker who came in
contact with asbestos in his

patients 1-0, 8-0, and 10-0
had mesothelioma; the oth-

er patient 1-N was a 65-
year-old man who had any occupa-

asbestos exposure. Her work was always
industrial; she was born and lived until the age
of 3, in the immediate neighborhood of an as-
bestos 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 as-
bestos 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 manufactur-
ing workers.

Patient 3-N never had any occupational as-
bestos 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 dis-
tributor, 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 as-
bestos textile plant. The exposure of these two
cases is questionable.

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

**Mesothelioma Patients With Family Con-
tacts 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 annu-
ally.

Patient 2-F, a 40-year-old nurse, never had
any occupational asbestos exposure, but her fa-
ther 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 pa-
tient 2-F pleural mesotheliomas.

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

Patient 1-Q was a welder for 35 years. Ac-
cording 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 no-
ticed. This boiler was covered with a friable as-
bestos insulation which flaked off on contact.

Patient 3-Q, a 14-year-old boy with mesothe-
lioma, had no occupational contact with asbes-
tos 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 dur-
ing 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 expo-
sure. Extensive questioning revealed that, on
two occasions several years before, he applied
asbestos insulation to boilers in his home, mix-
ing 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 fil-
tered through pulp filters consisting essentially
of cotton fibers and asbestos. After each filtra-
tion this 'FILTERMASS' is removed, mangled,
and washed in clear, warm water, then bleach-
ed 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 as-
bestos 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.

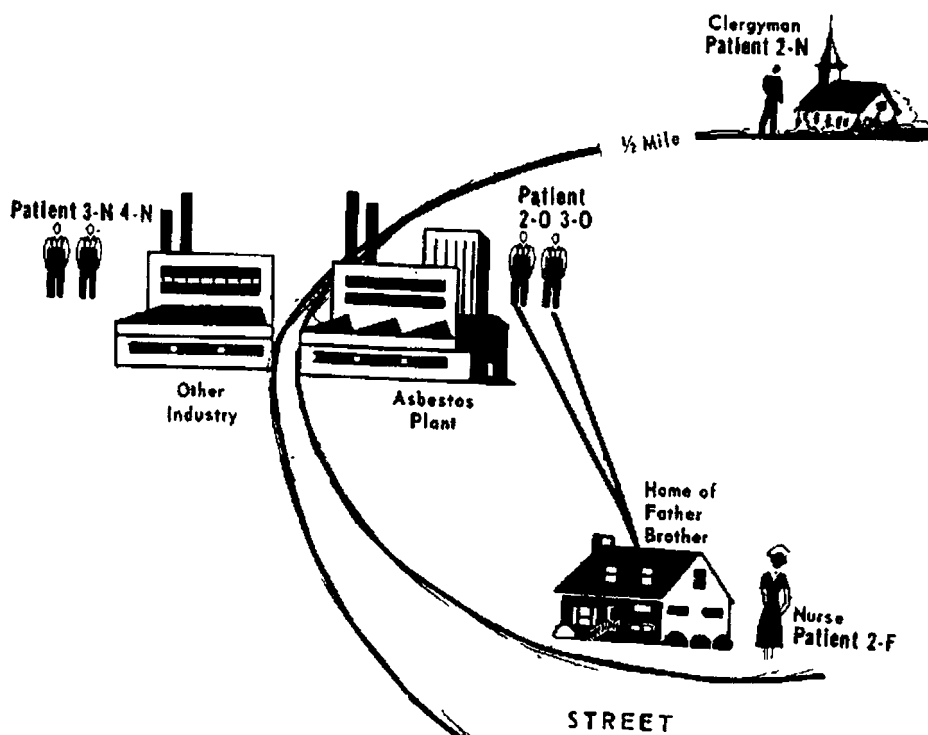
Comment

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.

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Nurse
Patient 2-F

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amely 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-O and 3-O), 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 story 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.