

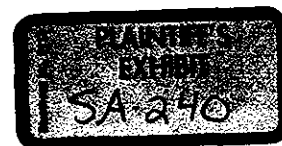
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MESOTHELIOMA OF PLEURA AND PERITONEUM FOLLOWING EXPOSURE TO ASBESTOS IN THE LONDON AREA

BY

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A series of 83 patients from the London Hospital with a diagnosis of mesothelioma confirmed by necropsy or biopsy has been studied for possible exposure to asbestos. The series consisted of 41 men and 42 women; 27 of the patients had peritoneal and 56 pleural tumours. The earliest death recorded was in 1917, but only 10 of the series died before 1950 and 40 (48%) between 1960 and 1964.

In 76 of the series full occupational and residential histories were obtained. Forty (52.6%) gave a history of occupational or domestic (living in the same house as an asbestos worker) exposure to asbestos compared with nine (11.8%) out of 76 patients from the same hospital suffering from other diseases ($P < 0.001$). None of the 17 suspected cases of mesothelioma, rejected on pathological grounds, was found to have had any exposure to asbestos. There was also evidence that neighbourhood exposures may be important. Among those with no evidence of occupational or domestic exposures, 30.6% of the mesothelioma patients and 7.6% of the in-patients with other diseases lived within half a mile of an asbestos factory ($P < 0.01$). Out of the 31 patients with occupational exposures only 10 were in jobs scheduled under the Asbestos Regulations of 1931. The interval between first exposure and the development of the terminal illness of mesothelioma ranged between 16 and 55 years.

In 47 patients in the mesothelioma series, lung tissue or sputum was available for examination. In 30 (62.5%), either asbestosis or asbestos bodies were present.

In recent years, the association between exposure to asbestos dust and cancer of the lung and other malignant neoplasms has been the subject of much research (leading article, 1964). Wagner, Sleggs, and Marchand (1960) described the occurrence of mesothelioma of the pleura in those exposed to crocidolite asbestos in the mining districts of South Africa, and this has stimulated further studies of the occupational histories of patients suffering from this tumour (Owen, 1964; Fowler, Sloper, and Warner, 1964). The present investigation concerns patients in whom mesothelioma had been diagnosed at the London Hospital during the past 50 years. After examining the necropsy and biopsy specimens held in the pathology department, Hourihane (1964) confirmed a diagnosis of mesothelioma in 83 patients, of whom 41 were men and 42 women. Thirty-one of the men had pleural tumours and 10 peritoneal;

among the women, 25 had pleural and 17 peritoneal tumours.

The aim of this study has been to establish the occupational histories of these patients and to trace any other possible exposure to asbestos. There were four surviving patients at the outset of the investigation, but these have subsequently died. The earliest date of death in the series was 1917; 10 died before 1950, 33 between 1950 and 1959, and the remaining 40 in the past four and a half years. The youngest patient died at the age of 33, and nearly half were dead before the age of 55 (Table 1).

Clinical Features

The ward notes of 65 of the patients were available and give a picture of a disease with a consistent symptomatology. Among those with pleural

TABLE 1
AGE AT DEATH OF 83 PATIENTS WITH MESOTHELIAL TUMOURS

Age (yr.)	Male		Female	
	No.	%	No.	%
<34	2	4.9	1	2.4
35-44	7	17.1	6	14.3
45-54	15	36.6	9	21.4
55-64	10	24.4	13	30.9
65+	7	17.1	3	19.0

tumours, the commonest presenting symptom was the rapid onset of extreme shortness of breath due to the formation of a massive pleural effusion. Pain was a prominent feature, either described as a dull ache, sometimes due to invasion of the ribs or vertebrae, or sometimes sharp and radiating, suggesting nerve involvement. Tumours in the chest wall were not uncommon, occurring either in previous operation scars or by direct invasion of the chest wall. The symptomatology of the peritoneal tumours was more varied. In some patients the presenting symptom was pain on defaecation or micturition. Diffuse upper abdominal pain was very common, and swelling of the abdomen due to ascites was always present terminally. The methods of treatment included pneumonectomy, decortication of the lung, deep x-ray therapy, instillation of radioactive gold, and cytotoxic drugs. They were used alone or in combination but had little effect on the course of the disease. Half of the patients suffering from pleural mesothelioma died within one year of the onset of symptoms, a further third within two years, and only one patient survived for more than three years. The course of those with peritoneal tumours appeared to be equally rapid. Eight of the patients died within six months of the onset of symptoms.

Sources of Information on Occupation and Residence

In addition to the ward notes, some of which gave good occupational histories, there were three other sources of information: the patient's general practitioner; the records of an asbestos factory in the area; and personal interviews with patients or their surviving relatives.

As a first step, general practitioners were circulated with an explanatory letter asking them to complete a form giving details of the occupations of patients and their immediate relatives. Within two months 65% of the doctors had replied. In two cases a hitherto unknown exposure to asbestos was revealed; in others the name and address of a surviving relative were given, but in the majority the doctor was unable to give information because, on the death of the

patient, the notes had been returned to the local executive council of the National Health Service, where they were destroyed within a period of three years.

In one of the asbestos factories a file was kept with detailed records of all employees since it started in 1913. The names of all patients were checked with these files. Nine men and nine married women (after their maiden names had been ascertained from relatives) were identified without difficulty. The exact dates of employment of these 18 patients and the jobs they had done were obtained from the records of the factory.

The four patients alive at the beginning of the investigation were interviewed personally. A few relatives were contacted by post, but the relatives of 68 patients were interviewed by one of us (H.T.) at their homes situated mostly in the East End of London. Not only was an occupational history of the patient, the spouse, sons and daughters, and father taken, but past addresses were also recorded. The interviews lasted for at least an hour. To recall events of 30 or 40 years ago it was often necessary to explore the residential and occupational histories of all members of the family.

Exposure to Asbestos in Three Groups of Patients Suffering from Other Diseases

For comparison with the mesothelioma patients, three further groups of patients suffering from other diseases were investigated.

The first group was selected from the patients in the medical and surgical wards of the hospital during the early summer of 1964 ('in-patient' series). Each patient in the mesothelioma series who had been traced was matched with an in-patient of the same sex born in the same five-year period. As there was a dearth of male patients over 75 years of age in the hospital, a sample of six patients of this age and older was taken from a neighbouring geriatric hospital.

The second group were those who had originally been filed in the pathology department of the hospital as cases of mesothelioma but in whom the diagnosis was subsequently rejected on pathological grounds by Hourihane (1964) ('rejected series'). As it had proved extremely difficult to locate the relatives of those who died before 1950, attempts were made only to trace the three survivors in this group and the 14 who died after 1950.

The in-patient series, already described, were all admitted to hospital in 1964. The patients with mesothelioma were admitted to the same hospital over a period of 47 years during which there might have been a substantial change both in the residential

areas and social conditions of London Hospital. was taken from the date of admission with the patients in places of residence for comparison with

Details of the series are given in about past domestic available for seven 6, 40 (52.6%) gave compared with on series (Table 2). 1

TYPES OF EXPOSURE WITH MESOTHELIO

Type of Exposure

Employed at one asbestos factory
Delivered goods to factories
Employed at other asbestos factories
Insulators and ladders
Relative worked with asbestos
Doctors handling asbestos
No history of work or domestic exposure to asbestos

Positive exposures positive histories in u

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statistically high (0.001). This res by the two grou year of admiss significant difference in the occupa and those adm during the con mesothelioma of the confirm gave a history This difference $\chi^2 = 11.83$; 1

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ages and social classes of patients attending the London Hospital. Thus, a third group of patients is taken from the hospital records matched by age of admission as well as date of birth and sex with the patients in the mesothelioma series. Their ages of residence and occupations were extracted in comparison with those of the in-patient series.

Results

Details of the 33 patients in the mesothelioma series are given in the Appendix. No information about past domestic and occupational histories was available for seven patients. Among the remaining 26 (52.6%) gave a history of exposure to asbestos compared with only nine (11.8%) of the 'in-patient' series (Table 2). The difference in this proportion is

TABLE 2

TYPES OF EXPOSURE TO ASBESTOS OF 26 PATIENTS WITH MESOTHELIOMA AND 26 IN-PATIENTS WITH OTHER DISEASES

Type of Exposure	Mesothelioma Series		'In-patient' Series	
	No.	%	No.	%
Employed at one asbestos factory	18	25.0	1	1.3
Delivered goods to factory	1			
Employed at other asbestos factories	4	5.3	1	1.3
Painters and ladders	8	10.5	4	5.3
Relative worked with asbestos	9	11.8	1	1.3
Dockers handling asbestos cargo	0	—	2	2.6
No history of work or domestic exposure to asbestos	36	47.4	67	88.2

Positive exposures to asbestos in mesothelioma series versus positive histories in in-patient series:

$$\chi^2 = 27.11, P < 0.001$$

*Seven cases of mesothelioma could not be traced and are omitted from this table.

statistically highly significant ($\chi^2 = 27.11$; $P < 0.001$). This result is unlikely to be unduly influenced by the two groups of patients not being matched for year of admission to hospital, since there was no significant difference either in the areas of residence or in the occupations of the patients admitted in 1964 and those admitted between 1917 and 1964. Comparing the confirmed and rejected patients in the mesothelioma group who died after 1950, 36 (50%) of 72 confirmed and none of the 17 rejected cases had a history of exposure to asbestos (Table 3). This difference is statistically highly significant ($\chi^2 = 11.83$; $P < 0.001$).

TABLE 3

EXPOSURE TO ASBESTOS OF CONFIRMED AND REJECTED CASES OF MESOTHELIOMA SURVIVING AFTER JANUARY 1950

Exposure to Asbestos	Diagnosis of Mesothelioma	
	Confirmed	Rejected
Exposure positive	36	0
No work or domestic contact found	35	16
Untraced	1	1

$$\chi^2 = 11.83, P < 0.001$$

Mesothelioma Series

Occupational Exposures.—There are details available for the 18 mesothelioma patients who had worked at one asbestos factory which used crocidolite asbestos with small amounts of chrysotile and first introduced amosite in 1926. Eleven started work before 1933 (the year when the asbestos regulations controlling the manufacture of asbestos goods and the protection of asbestos workers became effective), and seven started work between the beginning of 1933 and the end of 1942. The occupations of these workers and the type of asbestos they used are shown in Table 4. All of the 17 for whom details were available had used crocidolite asbestos. Five of the occupations listed are not scheduled as

TABLE 4

JOBS OF 17 PATIENTS WITH MESOTHELIOMA EMPLOYED AT ONE ASBESTOS FACTORY

Statutory Obligations	Job	Male	Female	Material
Subject to regulations	Spinning	0	4	Crocidolite
	Carding	1	1	Crocidolite
	Clothing and weaving	1	0	Crocidolite, chrysotile, amosite
	Disintegrating and opening	2	1	Crocidolite, chrysotile, amosite
Not subject to regulations	Filter making for A.R.P. masks	2	0	Crocidolite
	Manufacturing of preformed pipe insulation	1	1	Crocidolite
	Manufacturing of brake linings	1	0	Crocidolite
	Rubber compounding	0	1	Crocidolite, chrysotile
	General labourer	1	0	Crocidolite, chrysotile, amosite

*Employment history not available for one female patient.

requiring medical supervision under the Asbestos Regulations (1931).

Four patients were working at other factories making all types of asbestos goods. One had been employed in a wagon works sawing asbestos sheets for partitions. Except for one, a woman employed in insulating electrodes with crocidolite, the types of asbestos used in these other factories are not known.

The eight heating engineers and ladders were all men. Three had been employed in dockyards on ship repairs, two in various types of lagging, one in a power station, one installing hospital sterilizing equipment, and one installing central heating. All were consistently employed on this type of work for more than 20 years, but, in some, exposure to asbestos was intermittent.

Domestic Exposures.—The group of nine, seven women and two men, whose relatives worked with asbestos, are of particular interest. The most usual history was that of the wife who washed her husband's dungarees or work clothes. In one instance a relative said that the husband, a docker, came home 'white with asbestos' every evening for three or four years and his wife brushed him down. The two men in this group, when boys of 8 or 9 years old, had sisters who were working at an asbestos factory. One of these girls worked as a spinner from 1925 to 1936. In 1946 she died of asbestosis. The press report of the inquest states: 'She used to return home from work with dust on her clothes'. Her brother had apparently no other exposure to asbestos; he started work as a shop assistant, then became a sawyer of iron girders until 1948 when he worked as a loader of groceries in the docks for five years (but never on dusty cargoes) and then returned to sawing iron girders. He died in 1956 of a pleural mesothelioma.

In-patient Series

Occupational and Domestic Exposures.—Two of this series had worked in asbestos factories and four had been employed as ladders. The husband of another was employed at an asbestos factory for three years, and two dockers in this group gave histories of handling asbestos cargoes from time to time throughout their working life.

The diagnoses of these patients have been grouped into seven categories (Table 5). The patients with a positive history of exposure are scattered throughout the various diagnostic groups, and there is no indication that exposure to asbestos could be related to the disease which had caused their admission.

Neighbourhood Exposures of Mesothelioma and In-patient Series.—The 36 patients with meso-

TABLE 5
DISEASE GROUPS OF PATIENTS IN THE IN-PATIENT SERIES

Disease Group	No. of Patients	No. with Exposure to Asbestos
Cardiovascular	21	3
Metabolic	9	0
Renculo-endothelial (including anaemias)	8	2
Gastro-intestinal (excluding cancers)	6	2
Respiratory (excluding cancers)	3	2
All neoplasms	18	7
Other	11	1
Total	76	9

thelioma and the 67 patients in the 'in-patient' series, who had neither an occupational exposure nor a relative living in the home working with asbestos, might have been exposed to asbestos dust because they lived in the immediate vicinity of an asbestos factory.

One factory, where more than one-fifth of the mesothelioma patients were employed, opened in 1913, having been situated nearer the centre of London for the previous seven years. There were three affected female patients living within half a mile of the factory during the time it was in production at its first site. When it opened they were children between 5 and 7 years old. At the present site, there were eight patients living within a half-mile radius of the factory. One man was born within a quarter of a mile of the factory and remained at the same address for 16 years. The other seven were women, and all except one were children when the factory opened. The seventh was 23 years of age and remained in the same house until she died 48 years later. She is the only patient who had neither occupational nor household exposure but in whom asbestos bodies were found in the lungs at necropsy.

Among the 'in-patient' series, one patient lived near the factory at its previous site and four others lived near its present site. One patient was 22 years old when she moved into the neighbourhood in 1915. She disliked it and, when interviewed, complained impartially about the dust from the asbestos factory and the rats in the house.

TABLE 6
RESIDENCE OF PATIENTS WITH NO OCCUPATIONAL OR DOMESTIC EXPOSURE TO ASBESTOS

Series	Lived Within 1 mile of Asbestos Factory		Lived More Than 1 mile from Asbestos Factory		Total
	No.	%	No.	%	
Mesothelioma	11	30.6	25	69.4	36
In-patient	5	7.5	62	92.5	67

$$\chi^2 = 7.85, p < 0.01$$

Thus, among the domestic exposures to patients in the mesothelioma series, the 'in-patient' series, of an asbestos factory, the difference in the proportion who lived in the neighbourhood had no other exposure was significant ($\chi^2 = 7.85$).

Date of First Exposure.—The 36 patients with mesothelioma had been exposed to asbestos dust for a period of time near the main source of exposure varied from less than 10 years to over 50 years. The mean (37.5 years) was significantly longer than that of the 67 workers, where the mean interval was shorter. The interval was shorter in the 'in-patient' series, where the mean was 10 years. Table 7 shows the distribution of first exposure to asbestos and death in each group.

RELATION BETWEEN TYPE OF EXPOSURE AND INTERVAL BETWEEN FIRST EXPOSURE AND DEATH

Type of Exposure

Factory work
Domestic
Ladders and insulator
Living in neighbourhood of factory

Varied between 10 years and 50 years. The interval between first exposure and death showed a significant difference between the two groups of factories, years in the other series.

Asbestos Bodies.—The 36 patients with mesothelioma series, all certified as such by the pathologist, revealed the presence of asbestos bodies in the lungs. Both asbestos bodies and ladders. Asbestos bodies were found in the lungs of 11 patients with mesothelioma and 5 patients in the in-patient series.

Thus, among those with no occupational or domestic exposures to asbestos, there are 11 (30.6%) patients in the mesothelioma series and five (7.6%) in the 'in-patient' series who lived within half a mile of an asbestos factory in the area (Table 6). The difference in the proportion of patients in the two series who lived in the vicinity of the factory and had no other exposure to asbestos is statistically significant ($\chi^2 = 7.35$; $P < 0.01$).

Date of First Exposure and Interval Before Death in Mesothelioma Series.—Fifty-one men and women had been exposed to asbestos, including those who lived near the main asbestos factory. The duration of exposure varied widely, ranging from two months to over 50 years. The interval between the first exposure and death varied between 16 and 55 years (mean 37.5 years). Among the group of factory workers, where exposure was probably heaviest, the interval was shortest. It was longest among the group living in the neighbourhood of the asbestos factories, where exposure to dust was probably lightest. Table 7 shows the mean age of each group at exposure and the mean of the interval before death in each group. Although the length of interval

Lung tissue was available in only four patients exposed either through relatives or by living in the neighbourhood of asbestos factories. In two, asbestos bodies were present in lung tissue but there was no evidence of asbestosis.

TABLE 8

EVIDENCE OF ASBESTOS BODIES OR ASBESTOSIS IN 47 CASES OF MESOTHELIOMA WITH LUNG TISSUE OR SPUTUM AVAILABLE FOR EXAMINATION

History of Contact with Asbestos	Asbestosis or Asbestos Bodies		Lung Tissue not Available
	Present	Absent	
Positive	22	6	23
Negative	4	8	13
Untraced	4	3	0
Total	30	17	36

Among the 12 patients in whom no definite contact with asbestos could be established, there was one, a merchant seaman from South Africa, whose lungs showed both asbestos bodies and asbestosis; he may have had contact either in South Africa or at sea, but his early history could not be established. There were three others in this group who had asbestos bodies in lung tissue without evidence of asbestosis.

Of the seven patients whose histories could not be traced, three had asbestos bodies and histological evidence of asbestosis and one had asbestosis alone.

TABLE 7

RELATION BETWEEN TYPE OF EXPOSURE AND LENGTH OF INTERVAL BEFORE DEATH IN 51 PATIENTS IN MESOTHELIOMA SERIES

Type of Exposure	No.	Mean Age at First Exposure (years)	Mean Interval between First Exposure and Death (years)
Factory work	23	22.5	29.4
Domestic	9	17.9	37.9
Laggers and insulators	8	15.6	38.4
Living in neighbourhood of factory	11	8.5	48.6

varied between 29.4 and 48.6 years, the mean age at death showed less variation; it was 50.6 years in the group of factory workers and between 55 and 57 years in the other groups.

Asbestos Bodies and Asbestosis in the Mesothelioma Series.—Of the 83 patients in the mesothelioma series, lung tissue was available for examination in forty-three. In four other patients, all certified as suffering from asbestosis, with no lung tissue available, examination of sputum during life revealed the presence of asbestos bodies (Table 8).

Asbestos bodies and histological evidence of asbestosis were found in 15 of the 24 factory workers and laggers. A further five showed evidence of either asbestos bodies or asbestosis.

Discussion

In the mesothelioma series there are 25 patients in whom no evidence of any exposure to asbestos could be found. A chief source of information was a history taken from a surviving relative. A surprising amount of information was obtained, but in some of those interviewed the memory may have been defective or they may not have known of short periods of exposure during the youth of the deceased. For example, one of the patients was eventually identified as having worked at a large asbestos factory for two months in 1941. This was before he married, and his widow did not know of this episode. It is of interest that asbestos bodies in the lungs were found in only four of this group, and it seems probable that among the remainder there were those who had had no exposure to asbestos.

In the mesothelioma series of patients, both industrial and non-industrial exposures were recognized. Among the men the exposure was predominantly industrial; 22 worked in asbestos factories or as laggers, two were exposed at home; and one lived near the asbestos factory. Among the women only 10 worked in asbestos factories, and a

further 17 had non-industrial exposures, seven in the home and 10 living near asbestos factories.

There is no evidence that the patients with peritoneal tumours differed in their type of exposure from the patients with pleural tumours. The proportion of positive findings of asbestos bodies or asbestosis was similar in both groups. A higher proportion of women, particularly among the factory workers, was affected by peritoneal tumours, but the difference between the sexes was not statistically significant.

The recent increase in the number of patients diagnosed at the hospital may be partly due to an increased interest in mesothelial tumours and partly to the long interval between first exposure and development of the tumour. Those exposed between 1915 and 1925 might be expected to die from about 1950 onwards. Asbestos imports to the United Kingdom have mounted steeply since 1932 (Leathart, 1964) and its uses are more widely diversified in industry. The increasing proportion of the population exposed to asbestos during the past 30 years may be expected to give rise to an increasing occurrence of mesothelial tumours.

The choice of groups for comparison with the mesothelioma series of patients was not ideal. The number of patients it was possible to trace in the 'rejected' series proved to be very small. The 'in-patient' series, although matched for date of birth and sex, differed from the mesothelioma series in that all were admitted to hospital during 1964. Neither of these groups could be interviewed without knowledge of the disease from which they were suffering. This could have led to bias with under-reporting of exposure to asbestos in the in-patient series. However, in the 'in-patient' series the actual patient was interviewed, and more detailed and reliable histories were obtained than was possible from the relatives of those who had died of mesothelial tumours. There was no evidence that, because of their more recent admission to hospital, the in-patient series was less

likely than the mesothelioma series to work in contact with asbestos or to live in closer proximity to asbestos factories.

There seems little doubt that the risk of mesothelioma may arise from both occupational and domestic exposures to asbestos. Wagner and others (1960) described patients with no exposure other than living as a child in the vicinity of the asbestos mines. A high incidence of asbestos plaques of the pleura has been found in the population living near an anthophyllite mine in Finland (Kiviluoto, 1960). More evidence is required of an increased risk to the population living in the neighbourhood of asbestos factories or other areas, such as dockyards, where asbestos is used in quantity.

We should like to thank Dr. D. O'B. Hourthane for his co-operation and for making the results of his investigations available to us.

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MESOTHELIOMA

Case No.	Site of Primary Tumour	Sex
Section A: Factory workers		
8	Pleura	M
19	Peritoneum	M
18	Peritoneum	F
24	Pleura	M
14	Peritoneum	F
16	Peritoneum	F
13	Peritoneum	F
11	Peritoneum	F
15	Peritoneum	F
9	Peritoneum	F
21	Pleura	M
12	Peritoneum	F
5	Peritoneum	M
7	Peritoneum	M
2	Pleura	M
20	Peritoneum	M
17	Pleura	M
6	Pleura	M
10	Peritoneum	M
1	Pleura	M
23	Pleura	M
3	Peritoneum	M
4	Peritoneum	M
Section B: Lagers and others		
25	Pleura	M
28	Pleura	M
22	Pleura	M
30	Pleura	M
27	Peritoneum	M
26	Peritoneum	M
31	Pleura	M
29	Pleura	M

Appendix opposite

APPENDIX
EIGHTY-THREE PATIENTS WITH MESOTHELIAL TUMOURS

No.	Site of Primary Tumour	Sex	Year of Birth	Year of First Exposure	Duration of Exposure (years)	Year of Death	How Diagnosed	Asbestos Bodies in Lung Tissue	Pathological Evidence of Asbestos in Lung Tissue	Survival from Initial Symptoms (months)	Relevant History
<i>Section A: Factory workers</i>											
8	Pleura	M	1901	1921	17	1938	Necropsy	Positive	Positive	?	Brake liner, boiler coverer, asbestos factory; mainly crocidolite
19	Peritoneum	M	1895	1919	22	1941	Necropsy	Positive	Positive	?	Disintegrator and other jobs, asbestos factory; amosite, crocidolite, chrysotile
18	Peritoneum	F	1908	1925	5	1947	Biopsy	Positive (sputum)	N/A	?	Sectional pipe maker, asbestos factory, certified asbestos; mainly crocidolite
24	Pleura	M	1880	1928	12	1950	Necropsy	Positive	Negative	9	Used asbestos boarding in railway carriage construction
14	Peritoneum	F	1891	1917	?	1951	Necropsy	Negative	Negative	?	Asbestos factory, job unknown
16	Peritoneum	F	1906	1922	7	1951	Biopsy	Positive (sputum)	N/A	?	Owner and sectional pipe maker, asbestos factory, certified asbestos; amosite, crocidolite, chrysotile
13	Peritoneum	F	1894	1915	5	1955	Necropsy	Positive	Positive	12	Spinner, asbestos factory, certified asbestos; mainly crocidolite
11	Peritoneum	F	1895	1917	1	1955	Biopsy	Positive (sputum)	N/A	3	Sectional pipe maker, asbestos factory, certified asbestos; mainly crocidolite
15	Peritoneum	F	1901	1918	11	1955	Biopsy	Positive (sputum)	N/A	6	Spinner, asbestos factory, certified asbestos; mainly crocidolite
9	Peritoneum	F	1897	1919	1	1956	Necropsy	Positive	Negative	3	Disintegrator, asbestos factory; amosite, crocidolite, chrysotile
21	Pleura	M	1893	1928	1	1957	Biopsy	N/A	N/A	18	Asbestos mixer, north England asbestos factory
12	Peritoneum	F	1918	1937	2	1958	Biopsy	N/A	N/A	18	Carder, asbestos factory; mainly crocidolite
5	Peritoneum	M	1908	1927	30	1938	Necropsy	Positive	Positive	18	Clothing and weaving, asbestos factory; amosite, crocidolite, chrysotile
7	Peritoneum	M	1925	1940	4	1958	Biopsy	N/A	N/A	3	Filter maker for A.R.P. masks, asbestos factory; mainly crocidolite
2	Pleura	M	1925	1941	1/6	1959	Biopsy	Negative	Negative	11	Filter maker for A.R.P. masks, asbestos factory; mainly crocidolite
20	Peritoneum	F	1907	1921	10	1959	Necropsy	Negative	Negative	?	Electrode coverer; crocidolite
	Pleura	F	1908	1924	1	1962	Biopsy	Positive	Negative	?	Spinner, asbestos factory; mainly crocidolite
	Pleura	M	1907	1942	10	1962	Necropsy	Positive	Positive	?	Delivered chemicals to asbestos factory; amosite, crocidolite, chrysotile
10	Peritoneum	F	1899	1923	11	1963	Biopsy	Positive	Negative	5	Spinner, asbestos factory; mainly crocidolite
1	Pleura	M	1899	1936	26	1963	Necropsy	Positive	Positive	7	Labourer, works and buildings, asbestos factory; amosite, crocidolite, chrysotile
23	Pleura	M	1908	1925	1	1963	Necropsy	Positive	Negative	8	Worked in yard of insulating contractors
3	Peritoneum	M	1911	1930	2	1963	Necropsy	Positive	Positive	6	Carder, asbestos factory; mainly crocidolite
4	Peritoneum	M	1917	1937	27	1964	Necropsy	Positive	Positive	24	Disintegrator and other jobs, asbestos factory; amosite, crocidolite, chrysotile
<i>Section B: Lagers and insulators</i>											
25	Pleura	M	1894	1888	53	1935	Necropsy	Negative	Negative	12	Worked in close proximity to boiler repurifier in dockyards
28	Pleura	M	1893	1910	22	1955	Biopsy	N/A	N/A	24	Boiler cleaner and stripper, dockyards
22	Pleura	M	1921	1937	22	1959	Necropsy	Positive	Positive	9	Boiler coverer and lagger in various firms
10	Pleura	M	1908	1922	39	1961	Biopsy	N/A	N/A	25	Erecting and fitting central heating
27	Peritoneum	M	1908	1922	36	1961	Necropsy	Positive	Positive	12	Boiler coverer and pipe insulator, contracting firm
26	Peritoneum	M	1911	1927	34	1961	Necropsy	Positive	Positive	13	Lagger and boiler coverer, various firms
31	Pleura	M	1897	1916	41	1962	Biopsy	N/A	N/A	8	Intermittently boiler lagger, ship repairs
29	Pleura	M	1912	1927	34	1962	Biopsy	N/A	N/A	10	Installation of hospital sterilizing equipment

(continued)

APPENDIX (continued)

EIGHTY-THREE PATIENTS WITH MESOTHELIAL TUMOURS

Case No.	Site of Primary Tumour	Sex	Year of Birth	Year of First Exposure	Duration of Exposure (years)	Year of Death	How Diagnosed	Asbestos Bodies in Lung Tissue	Pathological Evidence of Asbestosis in Lung Tissue	Survival from Initial Symptoms (months)	Relevant History
<i>Section C: Exposure of relatives</i>											
40	Pleura	M	1912	1925	11	1956	Biopsy	N/A	N/A	27	Elder sister worked as spinner in asbestos factory; died of asbestosis.
34	Pleura	F	1913	1919	2	1937	Biopsy	N/A	N/A	14	Elder sister employed as spinner; looked after patient as child.
38	Pleura	F	1895	1919	41	1960	Biopsy	N/A	N/A	15	For several years husband worked in ship's engine room, close proximity to lagging operations.
37	Pleura	F	1905	1925	14	1960	Biopsy	N/A	N/A	3	Husband worked as boiler coverer; overalls brought home for washing.
35	Peritoneum	F	1890	1921	21	1960	Necropsy	Positive	Negative	24	Husband foreman and executive in asbestos factory.
33	Pleura	F	1916	1930	4	1961	Necropsy	Negative	Negative	7	Husband a dockworker; frequently handled 'white' asbestos.
39	Pleura	M	1919	1928	2	1961	Biopsy	N/A	N/A	18	Elder sister worked as spinner in asbestos factory and suffers from asbestosis.
32	Pleura	F	1900	1941	5	1963	Biopsy	N/A	N/A	13	Daughter worked in asbestos factory for 5 years; patient washed her overalls.
36	Peritoneum	F	1889	1912	18	1963	Biopsy	N/A	N/A	15	Husband railway carriage builder; lined compartments with asbestos sheeting; work clothes washed at home.
<i>Section D: Neighbourhood cases</i>											
44	Pleura	F	1903	1913	7	1959	Biopsy	N/A	N/A	8	Lived within 1 mile of present site of asbestos factory.
48	Pleura	M	1922	1922	16	1960	Biopsy	N/A	N/A	17	Lived within 1 mile of present site of asbestos factory.
42	Pleura	F	1889	1913	48	1961	Biopsy	Positive	Negative	15	Lived within 100 yards of present site of asbestos factory.
50	Pleura	F	1903	1908	6	1961	Biopsy	N/A	N/A	13	Lived within 1 mile of old site of asbestos factory.
43	Pleura	F	1905	1913	13	1961	Biopsy	N/A	N/A	4	Lived within 1 mile of present site of asbestos factory.
47	Pleura	F	1917	1917	10	1961	Biopsy	N/A	N/A	16	Lived within 200 yards of present site of asbestos factory.
64	Pleura	F	1899	1907	6	1962	Biopsy	Negative	Negative	5	Lived within 1 mile of old site of asbestos factory.
71	Pleura	F	1899	1907	6	1962	Biopsy	N/A	N/A	12	Lived within 1 mile of old site of asbestos factory.
41	Pleura	F	1900	1913	32	1962	Biopsy	N/A	N/A	29	Lived within 1 mile of present site of asbestos factory.
45	Pleura	F	1900	1913	7	1962	Biopsy	N/A	N/A	9	Lived within 1 mile of present site of asbestos factory.
46	Pleura	F	1907	1913	7	1963	Biopsy	N/A	N/A	7	Lived within 1 mile of present site of asbestos factory.
<i>Section E: No history of contact with asbestos</i>											
65	Pleura	F	1900			1947	Necropsy	Positive	Negative	7	Worked as nursemaid to manager of gas works in East London; asbestos insulation used in works.
68	Peritoneum	F	1902			1954	Necropsy	Negative	Negative	5	Shorthand-typist and housewife; lived Ilford area.
49	Pleura	M	1895			1954	Biopsy	N/A	N/A	?	Baker's roundsman, army, general labourer, publican for 30 years in East End of London.
75	Pleura	F	1899			1955	Biopsy	N/A	N/A	?	Munitions work before marriage; then housewife; lived Waltham Abbey, Essex.
74	Peritoneum	F	1904			1955	Necropsy	Negative	Negative	27	Tailor and housewife in East End of London.
62	Pleura	M	1899			1955	Necropsy	Negative	Positive	28	Employed as lumen and greaser, Beckton gas works 36 years; persistent discharging sinus R. side of chest following empyema 1923, acute chest infection 1953; subsequent thoracoplasty but deteriorated from this date.

Case No.	Site of Primary Tumour	Sex
61	Peritoneum	M
54	Pleura	M
76	Pleura	F
58	Pleura	M
66	Pleura	F
57	Peritoneum	M
52	Pleura	M
63	Pleura	M
51	Pleura	M
59	Pleura	M
73	Pleura	F
70	Pleura	F
72	Peritoneum	F
55	Pleura	N
60	Peritoneum	N
67	Pleura	F
56	Pleura	N
69	Peritoneum	F
53	Pleura	N
<i>Section F: Untraced cases</i>		
78	Pleura	?
83	Pleura	?
81	Pleura	?
80	Pleura	?
82	Pleura	?
77	Peritoneum	?
79	Pleura	?

(continued)

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APPENDIX (continued)

EIGHTY-THREE PATIENTS WITH MESOTHELIAL TUMOURS

	Site of Primary Tumour	Sex	Year of Birth	Year of First Exposure	Duration of Exposure (years)	Year of Death	How Diagnosed	Asbestos Bodies in Lung Tissue	Pathological Evidence of Asbestosis in Lung Tissue	Survival from Initial Symptoms (months)	Relevant History
1	Peritoneum	M	1913			1955	Biopsy	N/A	N/A	8	Merchant seaman, cargoes from S. Africa 1930-32, no definite evidence of contact with asbestos; subsequently employed on cross-channel boats
2	Pleura	M	1904			1956	Biopsy	N/A	N/A	12	Labourer and builder, finally employed in tunnelling; lived in East End of London
3	Pleura	F	1916			1957	Biopsy	N/A	N/A	19	Employed remaking old sacks in Bow, previous content of sacks not ascertained; lived East End of London
4	Pleura	M	1891			1957	Biopsy	N/A	N/A	11	Garage hand, chauffeur, mechanic; lived Wolverhampton and Epping
5	Pleura	F	1898			1958	Biopsy	N/A	N/A	6	Worked as printing machinist before marriage, then as housewife until death; lived East End of London
6	Peritoneum	M	1879			1958	Biopsy	N/A	N/A	3	Stereotyper and printer; lived originally in East London, then moved to Ipswich
7	Pleura	M	1890			1959	Biopsy	N/A	N/A	12	Van boy, regular army, cutter and grinder; lived N.E. London and Dagenham
8	Pleura	M	1904			1960	Biopsy	N/A	N/A	18	Bricklayer, cement worker, postman; lived East End of London, moved to Hainault, Essex in 1931
9	Pleura	M	1910			1960	Necropsy	Negative	Negative	18	Filter and turner; lived principally in East End of London
10	Pleura	M	1911			1960	Necropsy	Positive	Positive	?	Coloured S. African merchant seaman, stoker at glass factory; possible contact with asbestos in S. Africa or at sea
11	Pleura	F	1887			1962	Necropsy	Negative	Negative	10	Lived until marriage in Wales, then housekeeper in S.W. London
12	Pleura	F	1888			1962	Biopsy	Negative	Negative	30	Machinist of celluloid collars, housewife and canteen worker; lived East London
13	Peritoneum	F	1898			1962	Biopsy	N/A	N/A	10	Machinist in hosiery trade, Nottingham, housewife; moved to London 1960
14	Pleura	M	1888			1962	Necropsy	Negative	Negative	2	Labourer, merchant seaman, docker, carried only meat
15	Peritoneum	M	1915			1962	Necropsy	Negative	Negative	54	Apprentice printer, barman, cook, and butcher. For 25 years before death lived East End of London
16	Pleura	F	1897			1963	Biopsy	N/A	N/A	29	Dressmaker and housewife; lived East End of London then Somerset
17	Pleura	M	1912			1963	Biopsy	N/A	N/A	24	Steel erector, army, steel erector, labourer and porter; lived East End of London
18	Peritoneum	F	1901			1964	Necropsy	Negative	Negative	42	Employed as packer in pharmaceutical firm for 12 years, then housewife until death; lived in Dagenham
19	Pleura	M	1892			1964	Necropsy	Positive	Negative	24	Fisherman, fireman, docker, 1915-19 at Tilbury docks, fireman and finally storekeeper; contact with asbestos not probable at Tilbury docks; lived Tilbury area
Section F: Untraced cases											
20	Pleura	F	1893			1917	Necropsy	?	Positive		Not traced
21	Pleura	M	1860			1922	Necropsy	Negative	Negative		Not traced
22	Pleura	M	1877			1923	Necropsy	Negative	Negative		Not traced
23	Pleura	M	1900			1936	Necropsy	Negative	Negative		Not traced
24	Pleura	M	1893			1938	Necropsy	Positive	Positive		Not traced
25	Peritoneum	F	1910			1945	Necropsy	Positive	Positive		Not traced
26	Pleura	F	1878			1955	Necropsy	Positive	Positive		Not traced

N/A = tissue not available.

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MESOTHELIOMA OF PLEURA AND PERITONEUM FOLLOWING EXPOSURE TO ASBESTOS IN THE LONDON AREA

BY

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A series of 83 patients from the London Hospital with a diagnosis of mesothelioma confirmed by necropsy or biopsy has been studied for possible exposure to asbestos. The series consisted of 41 men and 42 women; 27 of the patients had peritoneal and 56 pleural tumours. The earliest death recorded was in 1917, but only 10 of the series died before 1950 and 40 (48%) between 1960 and 1964.

In 76 of the series full occupational and residential histories were obtained. Forty (52.6%) gave a history of occupational or domestic (living in the same house as an asbestos worker) exposure to asbestos compared with nine (11.8%) out of 76 patients from the same hospital suffering from other diseases ($P < 0.001$). None of the 17 suspected cases of mesothelioma, rejected on pathological grounds, was found to have had any exposure to asbestos. There was also evidence that neighbourhood exposures may be important. Among those with no evidence of occupational or domestic exposures, 30.6% of the mesothelioma patients and 7.6% of the in-patients with other diseases lived within half a mile of an asbestos factory ($P < 0.01$). Out of the 31 patients with occupational exposures only 10 were in jobs scheduled under the Asbestos Regulations of 1931. The interval between first exposure and the development of the terminal illness of mesothelioma ranged between 16 and 55 years.

In 47 patients in the mesothelioma series, lung tissue or sputum was available for examination. In 30 (62.5%), either asbestosis or asbestos bodies were present.

In recent years, the association between exposure to asbestos dust and cancer of the lung and other malignant neoplasms has been the subject of much research (leading article, 1964). Wagner, Sleggs, and Marchand (1960) described the occurrence of mesothelioma of the pleura in those exposed to crocidolite asbestos in the mining districts of South Africa, and this has stimulated further studies of the occupational histories of patients suffering from this tumour (Owen, 1964; Fowler, Sloper, and Warner, 1964).

The present investigation concerns patients in whom mesothelioma had been diagnosed at the London Hospital during the past 50 years. After examining the necropsy and biopsy specimens held in the pathology department, Hourihane (1964) confirmed a diagnosis of mesothelioma in 83 patients, of whom 41 were men and 42 women. Thirty-one of the men had pleural tumours and 10 peritoneal;

among the women, 25 had pleural and 17 peritoneal tumours.

The aim of this study has been to establish the occupational histories of these patients and to trace any other possible exposure to asbestos. There were four surviving patients at the outset of the investigation, but these have subsequently died. The earliest date of death in the series was 1917; 10 died before 1950, 33 between 1950 and 1959, and the remaining 40 in the past four and a half years. The youngest patient died at the age of 33, and nearly half were dead before the age of 55 (Table 1).

Clinical Features

The ward notes of 65 of the patients were available and give a picture of a disease with a consistent symptomatology. Among those with pleural

TABLE I
AGE AT DEATH OF 83 PATIENTS WITH MESOTHELIAL
TUMOURS

Age (yr.)	Male		Female	
	No.	%	No.	%
<34	2	4.9	1	2.4
35-44	7	17.1	6	14.3
45-54	15	36.4	9	21.4
55-64	10	24.4	18	42.9
65+	7	17.1	8	19.0

tumours, the commonest presenting symptom was the rapid onset of extreme shortness of breath due to the formation of a massive pleural effusion. Pain was a prominent feature, either described as a dull ache, sometimes due to invasion of the ribs or vertebrae, or sometimes sharp and radiating, suggesting nerve involvement. Tumours in the chest wall were not uncommon, occurring either in previous operation scars or by direct invasion of the chest wall. The symptomatology of the peritoneal tumours was more varied. In some patients the presenting symptom was pain on defaecation or micturition. Diffuse upper abdominal pain was very common, and swelling of the abdomen due to ascites was always present terminally. The methods of treatment included pneumonectomy, decortication of the lung, deep x-ray therapy, instillation of radioactive gold, and cytotoxic drugs. They were used alone or in combination but had little effect on the course of the disease. Half of the patients suffering from pleural mesothelioma died within one year of the onset of symptoms, a further third within two years, and only one patient survived for more than three years. The course of those with peritoneal tumours appeared to be equally rapid. Eight of the patients died within six months of the onset of symptoms.

Sources of Information on Occupation and Residence

In addition to the ward notes, some of which gave good occupational histories, there were three other sources of information: the patient's general practitioner; the records of an asbestos factory in the area; and personal interviews with patients or their surviving relatives.

As a first step, general practitioners were circulated with an explanatory letter asking them to complete a form giving details of the occupations of patients and their immediate relatives. Within two months 65% of the doctors had replied. In two cases a hitherto unknown exposure to asbestos was revealed: in others the name and address of a surviving relative were given, but in the majority the doctor was unable to give information because, on the death of the

patient, the notes had been returned to the local executive council of the National Health Service, where they were destroyed within a period of three years.

In one of the asbestos factories a file was kept with detailed records of all employees since it started in 1913. The names of all patients were checked with these files. Nine men and nine married women (after their maiden names had been ascertained from relatives) were identified without difficulty. The exact dates of employment of these 18 patients and the jobs they had done were obtained from the records of the factory.

The four patients alive at the beginning of the investigation were interviewed personally. A few relatives were contacted by post, but the relatives of 68 patients were interviewed by one of us (H.T.) at their homes situated mostly in the East End of London. Not only was an occupational history of the patient, the spouse, sons and daughters, and father taken, but past addresses were also recorded. The interviews lasted for at least an hour. To recall events of 30 or 40 years ago it was often necessary to explore the residential and occupational histories of all members of the family.

Exposure to Asbestos in Three Groups of Patients Suffering from Other Diseases

For comparison with the mesothelioma patients, three further groups of patients suffering from other diseases were investigated.

The first group was selected from the patients in the medical and surgical wards of the hospital during the early summer of 1964 ('in-patient' series). Each patient in the mesothelioma series who had been traced was matched with an in-patient of the same sex born in the same five-year period. As there was a dearth of male patients over 75 years of age in the hospital, a sample of six patients of this age and older was taken from a neighbouring geriatric hospital.

The second group were those who had originally been filed in the pathology department of the hospital as cases of mesothelioma but in whom the diagnosis was subsequently rejected on pathological grounds by Hourihane (1964) ('rejected series'). As it had proved extremely difficult to locate the relatives of those who died before 1950, attempts were made only to trace the three survivors in this group and the 14 who died after 1950.

The in-patient series, already described, were all admitted to hospital in 1964. The patients with mesothelioma were admitted to the same hospital over a period of 47 years during which there might have been a substantial change both in the residential

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areas and social classes of patients attending the London Hospital. Thus, a third group of patients was taken from the hospital records matched by date of admission as well as date of birth and sex with the patients in the mesothelioma series. Their places of residence and occupations were extracted for comparison with those of the in-patient series.

Results

Details of the 83 patients in the mesothelioma series are given in the Appendix. No information about past domestic and occupational histories was available for seven patients. Among the remaining 76, 40 (52.6%) gave a history of exposure to asbestos compared with only nine (11.8%) of the 'in-patient' series (Table 2). The difference in this proportion is

TABLE 2

TYPES OF EXPOSURE TO ASBESTOS OF 76* PATIENTS WITH MESOTHELIOMA AND 76 IN-PATIENTS WITH OTHER DISEASES

Type of Exposure	Mesothelioma Series		'In-patient' Series	
	No.	%	No.	%
Employed at one asbestos factory derived goods to factory	18	23.0	1	1.3
Employed at other asbestos factories	4	5.3	1	1.3
Insulators and ladders	2	2.6	4	5.3
Relative worked with asbestos	9	11.8	1	1.3
Dealers handling asbestos cargo	0	—	2	2.6
No history of work or domestic exposure to asbestos	36	47.4	67	88.2

*Positive exposures to asbestos in mesothelioma series versus passive histories in in-patient series.

$$\chi^2 = 27.11, P < 0.001$$

*Seven cases of mesothelioma could not be traced and are omitted from this table.

statistically highly significant ($\chi^2 = 27.11; P < 0.001$). This result is unlikely to be unduly influenced by the two groups of patients not being matched for year of admission to hospital, since there was no significant difference either in the areas of residence or in the occupations of the patients admitted in 1964 and those admitted between 1917 and 1964. Comparing the confirmed and rejected patients in the mesothelioma group who died after 1950, 36 (50%) of the confirmed and none of the 17 rejected cases gave a history of exposure to asbestos (Table 3). This difference is statistically highly significant ($\chi^2 = 11.83; P < 0.001$).

TABLE 3

EXPOSURE TO ASBESTOS OF CONFIRMED AND REJECTED CASES OF MESOTHELIOMA SURVIVING AFTER JANUARY 1950

Exposure to Asbestos	Diagnosis of Mesothelioma	
	Confirmed	Rejected
Exposure positive	36	0
No work or domestic contact found	33	16
Untraced	1	1

$$\chi^2 = 11.83, P < 0.001$$

Mesothelioma Series

Occupational Exposures.—There are details available for the 18 mesothelioma patients who had worked at one asbestos factory which used crocidolite asbestos with small amounts of chrysotile and first introduced amosite in 1926. Eleven started work before 1933 (the year when the asbestos regulations controlling the manufacture of asbestos goods and the protection of asbestos workers became effective), and seven started work between the beginning of 1933 and the end of 1942. The occupations of these workers and the type of asbestos they used are shown in Table 4. All of the 17 for whom details were available had used crocidolite asbestos. Five of the occupations listed are not scheduled as

TABLE 4

JOBS OF 17* PATIENTS WITH MESOTHELIOMA EMPLOYED AT ONE ASBESTOS FACTORY

Statutory Obligations	Job	Male	Female	Material
Subject to regulations	Spinning	0	4	Crocidolite
	Carding	1	1	Crocidolite
	Clothing and weaving	1	0	Crocidolite, chrysotile, amosite
	Disintegrating and opening	2	1	Crocidolite, chrysotile, amosite
Not subject to regulations	Filter making for A.R.P. masks	2	0	Crocidolite
	Manufacturing of preformed, pure insulation	1	1	Crocidolite
	Manufacturing of brake linings	1	0	Crocidolite
	Rubber compounding	0	1	Crocidolite, chrysotile
	General labourer	1	0	Crocidolite, chrysotile, amosite

*Employment history not available for one female patient.

requiring medical supervision under the Asbestos Regulations (1931).

Four patients were working at other factories making all types of asbestos goods. One had been employed in a wagon works sawing asbestos sheets for partitions. Except for one, a woman employed in insulating electrodes with crocidolite, the types of asbestos used in these other factories are not known.

The eight heating engineers and ladders were all men. Three had been employed in dockyards on ship repairs, two in various types of lagging, one in a power station, one installing hospital sterilizing equipment, and one installing central heating. All were consistently employed on this type of work for more than 20 years, but, in some, exposure to asbestos was intermittent.

Domestic Exposures.—The group of nine, seven women and two men, whose relatives worked with asbestos, are of particular interest. The most usual history was that of the wife who washed her husband's dungarees or work clothes. In one instance a relative said that the husband, a docker, came home 'white with asbestos' every evening for three or four years and his wife brushed him down. The two men in this group, when boys of 8 or 9 years old, had sisters who were working at an asbestos factory. One of these girls worked as a spinner from 1925 to 1936. In 1946 she died of asbestosis. The press report of the inquest states: 'She used to return home from work with dust on her clothes'. Her brother had apparently no other exposure to asbestos; he started work as a shop assistant, then became a sawyer of iron girders until 1948 when he worked as a loader of groceries in the docks for five years (but never on dusty cargoes) and then returned to sawing iron girders. He died in 1956 of a pleural mesothelioma.

In-patient Series

Occupational and Domestic Exposures.—Two of this series had worked in asbestos factories and four had been employed as ladders. The husband of another was employed at an asbestos factory for three years, and two dockers in this group gave histories of handling asbestos cargoes from time to time throughout their working life.

The diagnoses of these patients have been grouped into seven categories (Table 5). The patients with a positive history of exposure are scattered throughout the various diagnostic groups, and there is no indication that exposure to asbestos could be related to the disease which had caused their admission.

Neighbourhood Exposures of Mesothelioma and In-patient Series.—The 36 patients with meso-

TABLE 5
DISEASE GROUPS OF PATIENTS IN THE IN-PATIENT SERIES

Disease Group	No. of Patients	No. with Exposure to Asbestos
Cardiovascular	21	3
Mesothelioma	9	0
Respiratory (including anaemias)	8	2
Gastro-intestinal (excluding cancers)	4	2
Respiratory (excluding cancers)	3	0
All neoplasms	18	1
Other	11	1
Total	76	9

thelioma and the 67 patients in the 'in-patient' series, who had neither an occupational exposure nor a relative living in the home working with asbestos, might have been exposed to asbestos dust because they lived in the immediate vicinity of an asbestos factory.

One factory, where more than one-fifth of the mesothelioma patients were employed, opened in 1913, having been situated nearer the centre of London for the previous seven years. There were three affected female patients living within half a mile of the factory during the time it was in production at its first site. When it opened they were children between 5 and 7 years old. At the present site, there were eight patients living within a half-mile radius of the factory. One man was born within a quarter of a mile of the factory and remained at the same address for 16 years. The other seven were women, and all except one were children when the factory opened. The seventh was 23 years of age and remained in the same house until she died 48 years later. She is the only patient who had neither occupational nor household exposure but in whom asbestos bodies were found in the lungs at necropsy.

Among the 'in-patient' series, one patient lived near the factory at its previous site and four others lived near its present site. One patient was 22 years old when she moved into the neighbourhood in 1915. She disliked it and, when interviewed, complained impartially about the dust from the asbestos factory and the rats in the house.

TABLE 6
RESIDENCE OF PATIENTS WITH NO OCCUPATIONAL OR DOMESTIC EXPOSURE TO ASBESTOS

Series	Lived Within 1 mile of Asbestos Factory		Lived More Than 1 mile from Asbestos Factory		Total
	No.	%	No.	%	
Mesothelioma	11	30.6	25	69.4	36
In-patient	5	7.5	62	92.5	67

$$\chi^2 = 7.85, P < 0.01$$

MESOTHELIOMA OF PLEURA FOLLOWING EXPOSURE TO ASBESTOS

Thus, among those with no occupational or domestic exposures to asbestos, there are 11 (30.6%) patients in the mesothelioma series and five (7.6%) in the 'in-patient' series who lived within half a mile of an asbestos factory in the area (Table 6). The difference in the proportion of patients in the two series who lived in the vicinity of the factory and had had no other exposure to asbestos is statistically significant ($\chi^2 = 7.85$; $p < 0.01$).

Date of First Exposure and Interval Before Death in Mesothelioma Series.—Fifty-one men and women had been exposed to asbestos, including those who lived near the main asbestos factory. The duration of exposure varied widely, ranging from two months to over 50 years. The interval between the first exposure and death varied between 16 and 55 years (mean 37.5 years). Among the group of factory workers, where exposure was probably heaviest, the interval was shortest. It was longest among the group living in the neighbourhood of the asbestos factories, where exposure to dust was probably lowest. Table 7 shows the mean age of each group at first exposure and the mean of the interval before death in each group. Although the length of interval

TABLE 7

RELATION BETWEEN TYPE OF EXPOSURE AND LENGTH OF INTERVAL BEFORE DEATH IN 51 PATIENTS IN MESOTHELIOMA SERIES

Type of Exposure	No.	Mean Age at First Exposure (years)	Mean Interval between First Exposure and Death (years)
Factory work	23	23.5	29.4
Domestic	9	17.9	37.9
Laggers and insulators	8	15.4	38.4
Living in neighbourhood of factory	11	8.5	48.6

varied between 29.4 and 48.6 years, the mean age at death showed less variation: it was 50.6 years in the group of factory workers and between 55 and 57 years in the other groups.

Asbestos Bodies and Asbestosis in the Mesothelioma Series.—Of the 83 patients in the mesothelioma series, lung tissue was available for examination in forty-three. In four other patients, all certified as suffering from asbestosis, with no lung tissue available, examination of sputum during life revealed the presence of asbestos bodies (Table 8). Both asbestos bodies and histological evidence of asbestosis were found in 15 of the 24 factory workers and laggers. A further five showed evidence of either asbestos bodies or asbestosis.

Lung tissue was available in only four patients exposed either through relatives or by living in the neighbourhood of asbestos factories. In two, asbestos bodies were present in lung tissue but there was no evidence of asbestosis.

TABLE 8

EVIDENCE OF ASBESTOS BODIES OR ASBESTOSIS IN 47 CASES OF MESOTHELIOMA WITH LUNG TISSUE OR SPUTUM AVAILABLE FOR EXAMINATION

History of Contact with Asbestos	Asbestosis or Asbestos Bodies		Lung Tissue not Available
	Present	Absent	
Positive	22	6	23
Negative	4	8	13
Untraced	4	3	9
Total	30	17	34

Among the 12 patients in whom no definite contact with asbestos could be established, there was one, a merchant seaman from South Africa, whose lungs showed both asbestos bodies and asbestosis; he may have had contact either in South Africa or at sea, but his early history could not be established. There were three others in this group who had asbestos bodies in lung tissue without evidence of asbestosis.

Of the seven patients whose histories could not be traced, three had asbestos bodies and histological evidence of asbestosis and one had asbestosis alone.

Discussion

In the mesothelioma series there are 25 patients in whom no evidence of any exposure to asbestos could be found. A chief source of information was a history taken from a surviving relative. A surprising amount of information was obtained, but in some of those interviewed the memory may have been defective or they may not have known of short periods of exposure during the youth of the deceased. For example, one of the patients was eventually identified as having worked at a large asbestos factory for two months in 1941. This was before he married, and his widow did not know of this episode. It is of interest that asbestos bodies in the lungs were found in only four of this group, and it seems probable that among the remainder there were those who had had no exposure to asbestos.

In the mesothelioma series of patients, both industrial and non-industrial exposures were recognized. Among the men the exposure was predominantly industrial; 22 worked in asbestos factories or as laggers, two were exposed at home, and one lived near the asbestos factory. Among the women only 10 worked in asbestos factories, and a

further 17 had non-industrial exposures, seven in the home and 10 living near asbestos factories.

There is no evidence that the patients with peritoneal tumours differed in their type of exposure from the patients with pleural tumours. The proportion of positive findings of asbestos bodies or asbestosis was similar in both groups. A higher proportion of women, particularly among the factory workers, was affected by peritoneal tumours, but the difference between the sexes was not statistically significant.

The recent increase in the number of patients diagnosed at the hospital may be partly due to an increased interest in mesothelial tumours and partly to the long interval between first exposure and development of the tumour. Those exposed between 1915 and 1925 might be expected to die from about 1950 onwards. Asbestos imports to the United Kingdom have mounted steeply since 1932 (Leathart, 1964) and its uses are more widely diversified in industry. The increasing proportion of the population exposed to asbestos during the past 30 years may be expected to give rise to an increasing occurrence of mesothelial tumours.

The choice of groups for comparison with the mesothelioma series of patients was not ideal. The number of patients it was possible to trace in the 'rejected' series proved to be very small. The 'in-patient' series, although matched for date of birth and sex, differed from the mesothelioma series in that all were admitted to hospital during 1964. Neither of these groups could be interviewed without knowledge of the disease from which they were suffering. This could have led to bias with under-reporting of exposure to asbestos in the in-patient series. However, in the 'in-patient' series the actual patient was interviewed, and more detailed and reliable histories were obtained than was possible from the relatives of those who had died of mesothelial tumours. There was no evidence that, because of their more recent admission to hospital, the in-patient series was less

likely than the mesothelioma series to work in contact with asbestos or to live in closer proximity to asbestos factories.

There seems little doubt that the risk of mesothelioma may arise from both occupational and domestic exposures to asbestos. Wagner and others (1960) described patients with no exposure other than living as a child in the vicinity of the asbestos mines. A high incidence of asbestos plaques of the pleura has been found in the population living near an anthophyllite mine in Finland (Kiviluoto, 1960). More evidence is required of an increased risk to the population living in the neighbourhood of asbestos factories or other areas, such as dockyards, where asbestos is used in quantity.

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Appendix opposite

APPENDIX
EIGHTY-THREE PATIENTS WITH MESOTHELIAL TUMOURS

No.	Site of Primary Tumour	Sex	Year of Birth	Year of First Exposure	Duration of Exposure (years)	Year of Death	How Diagnosed	Asbestos Bodies in Lung Tissue	Pathological Evidence of Asbestosis in Lung Tissue	Survival from Initial Symptoms (months)	Relevant History
Section A: Factory workers											
8	Pleura	M	1901	1921	17	1938	Necropsy	Positive	Positive	?	Brake liner, boiler coverer, asbestos factory; mainly crocidolite
19	Peritoneum	M	1895	1919	22	1941	Necropsy	Positive	Positive	?	Disintegrator and other jobs, asbestos factory; amosite, crocidolite, chrysotile
18	Peritoneum	F	1908	1925	5	1947	Biopsy	Positive (sputum)	N/A	?	Sectional pipe maker, asbestos factory, certified asbestosis; mainly crocidolite
24	Pleura	M	1880	1928	12	1950	Necropsy	Positive	Negative	9	Lined asbestos boarding in railway carriage construction
14	Peritoneum	F	1891	1917	?	1951	Necropsy	Negative	Negative	?	Asbestos factory, job unknown
16	Peritoneum	F	1906	1922	?	1951	Biopsy	Positive (sputum)	N/A	?	Owner and sectional pipe maker, asbestos factory, certified asbestosis; amosite, crocidolite, chrysotile
13	Peritoneum	F	1894	1915	5	1955	Necropsy	Positive	Positive	12	Spinner, asbestos factory, certified asbestosis; mainly crocidolite
11	Peritoneum	F	1895	1917	1	1955	Biopsy	Positive (sputum)	N/A	3	Sectional pipe maker, asbestos factory, certified asbestosis; mainly crocidolite
15	Peritoneum	F	1901	1918	11	1955	Biopsy	Positive (sputum)	N/A	6	Spinner, asbestos factory, certified asbestosis; mainly crocidolite
9	Peritoneum	F	1897	1919	1	1956	Necropsy	Positive	Negative	3	Disintegrator, asbestos factory; amosite, crocidolite, chrysotile
21	Pleura	M	1893	1928	1	1957	Biopsy	N/A	N/A	18	Asbestos mixer, north England asbestos factory
12	Peritoneum	F	1918	1937	2	1958	Biopsy	N/A	N/A	18	Carder, asbestos factory; mainly crocidolite
5	Peritoneum	M	1908	1927	30	1958	Necropsy	Positive	Positive	18	Clothing and weaving, asbestos factory; amosite, crocidolite, chrysotile
7	Peritoneum	M	1925	1940	4	1958	Biopsy	N/A	N/A	3	Filter maker for A.R.P. masks, asbestos factory; mainly crocidolite
2	Pleura	M	1925	1941	1/6	1959	Biopsy	Negative	Negative	11	Filter maker for A.R.P. masks, asbestos factory; mainly crocidolite
20	Peritoneum	F	1907	1921	10	1959	Necropsy	Negative	Negative	?	Electrode coverer; crocidolite
	Pleura	F	1908	1924	1	1962	Biopsy	Positive	Negative	?	Spinner, asbestos factory; mainly crocidolite
	Pleura	M	1907	1942	10	1962	Necropsy	Positive	Positive	?	Delivered chemicals to asbestos factory; amosite, crocidolite, chrysotile
10	Peritoneum	F	1899	1923	11	1963	Biopsy	Positive	Negative	5	Spinner, asbestos factory; mainly crocidolite
1	Pleura	M	1899	1936	26	1963	Necropsy	Positive	Positive	?	Labourer, works and buildings, asbestos factory; amosite, crocidolite, chrysotile
23	Pleura	M	1908	1925	1	1963	Necropsy	Positive	Negative	8	Worked in yard of insulating contractors
3	Peritoneum	M	1911	1930	2	1963	Necropsy	Positive	Positive	6	Carder, asbestos factory; mainly crocidolite
4	Peritoneum	M	1917	1937	27	1964	Necropsy	Positive	Positive	24	Disintegrator and other jobs, asbestos factory; amosite, crocidolite, chrysotile
Section B: Lagers and insulators											
25	Pleura	M	1874	1888	53	1935	Necropsy	Negative	Negative	12	Worked in close proximity to boiler repairer in dockyards
28	Pleura	M	1893	1910	22	1955	Biopsy	N/A	N/A	24	Boiler cleaner and stripper, dockyards
22	Pleura	M	1921	1937	22	1959	Necropsy	Positive	Positive	9	Boiler coverer and lagger to various firms
10	Pleura	M	1908	1922	39	1961	Biopsy	N/A	N/A	25	Erecting and fitting central heating
27	Peritoneum	M	1908	1922	36	1961	Necropsy	Positive	Positive	12	Boiler coverer and pipe insulator, contracting firm
26	Peritoneum	M	1911	1927	34	1961	Necropsy	Positive	Positive	13	Lagger and boiler coverer, various firms
31	Pleura	M	1897	1916	41	1962	Biopsy	N/A	N/A	8	Intermittently boiler lagger, ship repairs
29	Pleura	M	1912	1927	34	1962	Biopsy	N/A	N/A	10	Installation of hospital sterilizing equipment

(continued)

APPENDIX (continued)

EIGHTY-THREE PATIENTS WITH MESOTHELIAL TUMOURS

Case No.	Site of Primary Tumour	Sex	Year of Birth	Year of First Exposure	Duration of Exposure (years)	Year of Death	How Diagnosed	Asbestos Bodies in Lung Tissue	Pathological Evidence of Asbestosis in Lung Tissue	Survival from Initial Symptoms (months)	Relevant History
<i>Section C: Exposure of relatives</i>											
40	Pleura	M	1912	1925	11	1956	Biopsy	N/A	N/A	27	Elder sister worked as spin asbestos factory. died certified asbestotic
34	Pleura	F	1913	1919	2	1957	Biopsy	N/A	N/A	14	Elder sister employed as spin looked after patient as child
38	Pleura	F	1895	1919	41	1960	Biopsy	N/A	N/A	15	For several years husband was ship's engine room, proximity to lagging operation
37	Pleura	F	1905	1925	14	1960	Biopsy	N/A	N/A	3	Husband worked as boiler on overalls brought home for
35	Peritoneum	F	1890	1921	21	1960	Necropsy	Positive	Negative	24	Husband foreman and exec asbestos factory
33	Pleura	F	1916	1930	4	1961	Necropsy	Negative	Negative	7	Husband a docker; free handled white asbestos
39	Pleura	M	1919	1928	2	1961	Biopsy	N/A	N/A	18	Elder sister worked as spin asbestos factory and suffer asbestosis
32	Pleura	F	1900	1941	5	1963	Biopsy	N/A	N/A	18	Daughter worked in asbestos for 5 years; patient with overalls
36	Peritoneum	F	1889	1912	18	1963	Biopsy	N/A	N/A	15	Husband railway carriage lined compartments with sheeting; work clothes at home
<i>Section D: Neighbourhood cases</i>											
44	Pleura	F	1905	1913	7	1959	Biopsy	N/A	N/A	8	Lived within 1 mile of pre of asbestos factory
48	Pleura	M	1922	1922	16	1960	Biopsy	N/A	N/A	17	Lived within 1 mile of pre of asbestos factory
42	Pleura	F	1889	1913	48	1961	Biopsy	Positive	Negative	15	Lived within 100 yards of site of asbestos factory
50	Pleura	F	1903	1908	6	1961	Biopsy	N/A	N/A	13	Lived within 1 mile of asbestos factory
43	Pleura	F	1905	1913	13	1961	Biopsy	N/A	N/A	4	Lived within 1 mile of pre of asbestos factory
47	Pleura	F	1917	1917	10	1961	Biopsy	N/A	N/A	16	Lived within 200 yards of site of asbestos factory
64	Pleura	F	1899	1907	6	1962	Biopsy	Negative	Negative	5	Lived within 1 mile of asbestos factory
71	Pleura	F	1899	1907	6	1962	Biopsy	N/A	N/A	12	Lived within 1 mile of asbestos factory
41	Pleura	F	1900	1913	32	1962	Biopsy	N/A	N/A	29	Lived within 1 mile of pre of asbestos factory
45	Pleura	F	1900	1913	7	1962	Biopsy	N/A	N/A	9	Lived within 1 mile of pre of asbestos factory
46	Pleura	F	1907	1913	7	1963	Biopsy	N/A	N/A	7	Lived within 1 mile of pre of asbestos factory
<i>Section E: No history of contact with asbestos</i>											
45	Pleura	F	1900			1947	Necropsy	Positive	Negative	7	Worked as nursemaid in of gas works in East asbestos insulation used
68	Peritoneum	F	1902			1954	Necropsy	Negative	Negative	5	Shorthand typist and lived Ilford area
49	Pleura	M	1895			1954	Biopsy	N/A	N/A	7	Baker's roundsman, arm labourer, publican for East End of London
75	Pleura	F	1899			1955	Biopsy	N/A	N/A	7	Munitions work before then housewife; lived Abbey, Essex
74	Peritoneum	F	1904			1955	Necropsy	Negative	Negative	27	Tailor and housewife End of London
62	Pleura	M	1899			1955	Necropsy	Negative	Positive	23	Employed as fireman's Beckton gas works persistent discharging side of chest followed in 1925, acute chest inf., subsequent thoracic deteriorated from this

MESOTHELIOMA OF PLEURA FOLLOWING EXPOSURE

APPENDIX (continued)

EIGHTY-THREE PATIENTS WITH MESOTHELIAL TUMOURS

Case No.	Site of tumour	Sex	Year of Birth	Year of First Exposure	Duration of Exposure (years)	Year of Death	How Diagnosed	Asbestos bodies in Lung Tissue	Pathological Evidence of Asbestosis in Lung Tissue	Survival from Initial Symptoms (months)	Relevant History
	Peritoneum	M	1913			1955	Biopsy	N/A	N/A	8	Merchant seaman, cargoes from S. Africa 1930-32, no definite evidence of contact with asbestos; subsequently employed on cross-channel boats
	Pleura	M	1904			1956	Biopsy	N/A	N/A	12	Labourer and builder, finally employed in tunnelling; lived in Dept. End of London
	Pleura	F	1916			1957	Biopsy	N/A	N/A	19	Employed remaking old sacks in Bow, previous content of sacks not ascertained; lived East End of London
1	Pleura	M	1891			1957	Biopsy	N/A	N/A	11	Garage hand, chauffeur, mechanic; lived Wolverhampton and Lymington
6	Pleura	F	1898			1958	Biopsy	N/A	N/A	6	Worked as printing machines before marriage, then as housewife until death; lived East End of London
7	Peritoneum	M	1879			1958	Biopsy	N/A	N/A	3	Stereotypist and printer; lived originally in East London, then moved to Ipswich
12	Pleura	M	1890			1959	Biopsy	N/A	N/A	12	Van boy, regular army, cutter and grinder; lived N.E. London and Dagenham
13	Pleura	M	1904			1960	Biopsy	N/A	N/A	18	Bricklayer, cement worker, postman; lived East End of London, moved to Hainault, Essex in 1931
31	Pleura	M	1910			1960	Necropsy	Negative	Negative	18	Filter and turner; lived principally in East End of London
39	Pleura	M	1911			1960	Necropsy	Positive	Positive	?	Coloured S. African merchant seaman, stoker at glass factory; possible contact with asbestos in S. Africa or at sea
	Pleura	F	1887			1962	Necropsy	Negative	Negative	10	Lived until marriage in Wales, then housekeeper in S.W. London
	Pleura	F	1888			1962	Biopsy	Negative	Negative	30	Machinist of celluloid collars, housewife and canteen worker; lived East London
72	Peritoneum	F	1898			1962	Biopsy	N/A	N/A	10	Machinist in hosiery trade, Nottingham, housewife; moved to London 1940
	Peritoneum	M	1888			1962	Necropsy	Negative	Negative	2	Labourer, merchant seaman, docker, carried only meat
	Peritoneum	M	1915			1962	Necropsy	Negative	Negative	54	Apprentice printer, barman, cook, and butcher. For 25 years before death lived East End of London
67	Pleura	F	1897			1963	Biopsy	N/A	N/A	29	Dressmaker and housewife; lived East End of London then Somerset
56	Pleura	M	1912			1963	Biopsy	N/A	N/A	24	Steel erector, army, steel erector, labourer and porter; lived East End of London
69	Peritoneum	F	1901			1964	Necropsy	Negative	Negative	42	Employed as packer in pharmaceutical firm for 12 years, then housewife until death; lived in Dagenham
53	Pleura	M	1892			1964	Necropsy	Positive	Negative	24	Fisherman, fireman, docker, 1915-39 at Tilbury docks, fireman and finally storekeeper; contact with asbestos not probable at Tilbury docks; lived Tilbury area
Section F: Untraced cases											
78	Pleura	F	1893			1917	Necropsy	?	Positive		Not traced
83	Pleura	M	1860			1922	Necropsy	Negative	Negative		Not traced
1	Pleura	M	1877			1925	Necropsy	Negative	Negative		Not traced
30	Pleura	M	1900			1936	Necropsy	Negative	Negative		Not traced
12	Pleura	M	1893			1938	Necropsy	Positive	Positive		Not traced
77	Peritoneum	F	1910			1945	Necropsy	Positive	Positive		Not traced
17	Pleura	F	1878			1955	Necropsy	Positive	Positive		Not traced

N/A = tissue not available.