

Mesothelioma Register 1967-68

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Greenberg, M., and Lloyd Davies, T. A. (1974), *British Journal of Industrial Medicine*, 31, 91-104. Mesothelioma Register 1967-68. A register of mesothelioma cases is maintained by the Department of Employment, Medical Services Division (now Employment Medical Advisory Service). This paper describes an investigation of 413 notifications to the Register in 1967-68 from England and Wales and Scotland.

Cases were regarded as 'definite' when histological confirmation of diagnosis had been obtained, either by hospital pathologists, or by the UICC Panel of Pathologists, to whom pathological material was submitted whenever possible. Two hundred and forty-six cases were accepted as 'definite' and 76 cases were regarded as 'definitely not' mesothelioma. The remainder were classified as 'undecided' or 'insufficient pathological material'. Thirty-five of the 76 cases definitely not mesothelioma had nevertheless been so described on death certificates.

The investigation carried out covers clinical aspects, survival, and evidence of exposure to asbestos. Twelve per cent of definite mesotheliomata were of peritoneal origin. The age range was 21 to 87 years, but, in general, mesothelioma occurred at an earlier age than 'carcinoma of bronchus and lung' or 'all malignant tumours' in the Registrar General's statistical mortality tables.

Concomitant asbestosis and the finding of asbestos bodies or pleural plaques occurred as frequently in those cases classified as definitely not mesothelioma as in confirmed cases.

Occupational exposure to asbestos was found in 68% of definite cases, apparently significantly more frequently than in those definitely not mesothelioma, but there was observer bias. The interval between first exposure and death from mesothelioma exceeded 25 years in 85% of cases but was only three and a half years in one case. The duration of exposure varied widely; in 12% of cases it was under five years. The type of asbestos could be ascertained in so few cases that it was impossible to assess the rôle of crocidolite in aetiology. There were 38 definite cases in which no history of any exposure to asbestos could be obtained.

Definite mesotheliomata showed marked clustering in areas where there is substantial industrial use of asbestos. Whether this should be interpreted as evidence of causation or an effect of heightened awareness in these areas cannot be deduced from this study. Evidence is quoted suggesting that the observed annual incidence of approximately 120 definite mesotheliomata in England, Scotland, and Wales may considerably understate the true prevalence.

of malignant mesothelioma of the pleura and peritoneum, although rare, has been sought for increasingly in the past decade. The reported association with asbestos exposure (Wagner, Sleggs, and

Marchand, 1960) gave impetus to the enquiry. For some years the Pneumoconiosis Unit of the Medical Research Council had recorded cases of mesothelioma reported to them. By 1966 a register of some,

containing compounds, or where the subject worked in an atmosphere contaminated by asbestos dust.

'Possible', where the job description was too imprecise to be certain, but there was a strong suspicion of exposure to asbestos.

'None', where, after exhaustive enquiry, no occupational exposure could be presumed.

'Unknown', where adequate industrial details were not forthcoming. If possible the duration of exposure was recorded and the length of time before death that exposure ceased. The duration in intermittent exposures is presented as a cumulative figure.

Domestic exposure

Domestic exposure was considered as positive when a history that members of a subject's family had come home visibly contaminated by asbestos was obtained.

Hobby exposure

Hobby exposure was recorded in several householders or smallholders who gave a history of sawing asbestos sheeting for the construction of outhouses, garages, and chicken houses.

Neighbourhood exposure

Neighbourhood exposure was recorded when subjects lived within one mile of an asbestos factory or shipyard using asbestos but had no occupational exposure.

Other evidence of asbestos exposure

Asbestos exposure was presumed in cases showing evidence of asbestosis (either on chest radiograph or at necropsy) and in those in whom asbestos bodies

or fibres had been demonstrated by light microscopy in sputum, lung sections, or fluid expressed from the cut surface of the lung. The reported finding of pleural plaques at operation or necropsy, or evidence of plaques on the chest radiograph, was regarded as suggestive of asbestos exposure.

Results

For the years 1967 and 1968, a total of 413 cases was reported to the mesothelioma register. Of these, 168 were first notified by death certificate as having died in those years and a further 166 were notified in life and died during this period. Seventy-nine subjects notified survived the period of study.

Death certificates were the most important source of notification comprising 53.5% of all notifications in 1967 and 77.8% in 1968. In the absence of death certifications, further notifications were received from cancer bureaux, 45 (26.5%) in 1967 and 33 (13.6%) in 1968. Further groups of cases were reported exclusively by other sources (physicians, surgeons, and pathologists), 31 (18.2%) in 1967 and 18 (7.4%) in 1968. Three other cases otherwise unreported were reported in each year by the Pneumoconiosis Medical Panels. A total of 170 notifications were made in 1967 and 243 in 1968.

Pathological diagnosis

In Table 1 the notifications are shown categorized according to the criteria of diagnosis. The correlation between histological diagnosis and the diagnosis given on the death certificate was weak. Of the 246 cases accepted as 'definite', only 186 were so described on death certificates. On the other hand, of 76 cases 'definitely not mesothelioma' death had been attributed to mesothelioma on the death

TABLE 1
NOTIFICATIONS TO MESOTHELIOMA REGISTER ANALYSED BY DIAGNOSTIC CRITERIA AND SITE OF TUMOUR

	Site of tumour	Diagnostic category ¹				Total
		Definite	Undecided	Insufficient material	Definitely not	
UICC Panel	Pleura	118	14	12	23	167
	Peritoneum	16	4	1	7	28
Other pathologists	Pleura	98	26	32	42	198
	Peritoneum	14	2	0	4	20
Total	Pleura	216	40	44	65	365
	Peritoneum	30	6	1	11	48
All cases		246	46	45	76	413

¹ See text for definition

certificates in 35 instances. The pathological diagnoses in these 35 cases were:

Carcinoma of bronchus	11
Carcinoma, origin unstated	10
Secondary adenocarcinoma (primary unstated)	3
Not mesothelioma (no other diagnosis)	4
Myelomatosis	1
Transitional carcinoma of bladder	1
Adenocarcinoma of thyroid	1
Retroperitoneal fibroma or chordoma	1
Asbestosis and tuberculosis	1
Severe anaemia secondary to peptic ulcer	1
Malignant melanoma	1

As the concordance of diagnoses between the UICC pathology panel and other pathologists was higher than 74%, and the characteristics of the two groups are so similar for distribution of age at death (Fig. 1), tumour site, sex (Table 2), and survival (Figs 2 to 4), they can be treated as one. In this study

peritoneal tumour represented 12.2% of all confirmed mesotheliomas (Table 2). This compares with reported proportions by five authors with a range of 3.7% (of 80 cases) to 72.7% (of 22 cases) (Table 3). From Table 2 it can be seen that the distribution of cases between the sites was similar in the groups confirmed by UICC pathologists and by other pathologists.

Sex distribution

Table 2 shows that the ratio of mesothelioma in men and women for both UICC and other pathologists was about 5:1, which is similar to that for all malignant neoplasms of the respiratory system (Registrar General, 1970). The sex difference in carcinoma of the bronchus in general is thought in part to be due to difference in smoking habits (Hammond, 1966) but tobacco is not known to play a role in the aetiology of mesothelioma. If it is assumed that mesothelioma is related to asbestos

TABLE 2
246 'DEFINITE' MESOTHELIOMAS ANALYSED BY SEX AND SITE OF TUMOUR

Pathologists	Site of tumour	Males (% of all meso- thelial tumours)	Females (% of all meso- thelial tumours)	Total
UICC Panel	Pleural	96	22	118
	Peritoneal	14 (12.8%)	2 (8.3%)	16 (11.9%)
Other pathologists	Pleural	81	17	98
	Peritoneal	10 (10.9%)	4 (19.0%)	14 (12.5%)
All	Pleural	177	39	216
	Peritoneal	24 (12.0%)	6 (13.3%)	30 (12.2%)

TABLE 3
PREVALENCE OF PERITONEAL MESOTHELIOMAS REPORTED BY VARIOUS AUTHORS

Authors	All mesotheliomas	Peritoneal mesotheliomas only (total)	Comment
McEwen <i>et al.</i> (1970)	80	3 (3.7%)	73 males and 7 females; 2 males described as 'both sites' (Scotland)
Ashcroft and Heppleston (1970)	23	3 (13.0%)	Tyneside
Selikoff <i>et al.</i> (1970)	22	16 (72.7%)	Male insulation workers (USA)
Thomson (1970)	17	3 (17.6%)	Cape Town
Newhouse <i>et al.</i> (1972)	11	5 (45.4%)	Females (London)
	49	30 (61.2%)	Males from the same factory
Present study	246	30 (12.2%)	England, Wales and Scotland 1967-68

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TABLE 4
NOTIFICATIONS TO MESOTHELIOMA REGISTER
ANALYSED BY ASBESTOS EXPOSURE

Asbestos exposure history	No. of definite mesotheliomas	No. undecided, inadequate material, or definite alternative diagnoses
Definite occupational exposure	167	63
Possible occupational exposure	16	17
Neighbourhood, domestic or hobby	13	10
None	38	57
Not obtained	12	20

exposure it would be necessary to know the numbers of men and women at risk over the past 50 years in order to assess the relative susceptibility of the sexes to mesothelioma.

Age at death

The distribution of age at death of confirmed cases is presented in Fig. 1: there is no significant difference between cases diagnosed by the two groups of pathologists (mean age: UICC, 59.4 ± 0.9 ; other pathologists, 60.2 ± 1.3). For comparison the age distributions for all malignant neoplasms and for carcinoma of the bronchus and lung (Registrar General, 1970) are also shown. The mean age at death from mesothelioma is significantly younger ($P < 0.05$) than that for bronchial carcinoma and 'all neoplasms'. This may be due in part or in whole either to the greater chance of identifying occupational cancers within the working age compared with the retired or to earlier death from mesothelioma associated with occupational exposure to a carcinogen.

Exposure to asbestos

In Table 4 it can be seen that of 246 confirmed cases 167 (68%) had definite occupational exposure to asbestos and a further 29 were possibly exposed, either at work or at home. There were, however,

still 38 (15%) for whom careful enquiry failed to elicit any exposure whatever. In the remaining notifications ('undecided', 'inadequate material', 'definite alternative diagnosis') nearly one third were without apparent exposure, and those with definite occupational history formed only 38% of the total. The differences between these groups are significant ($P < 0.001$) but may be affected by bias towards

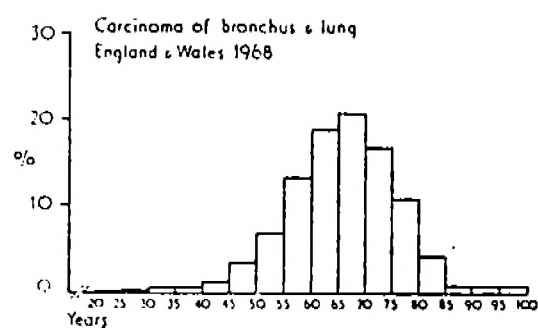
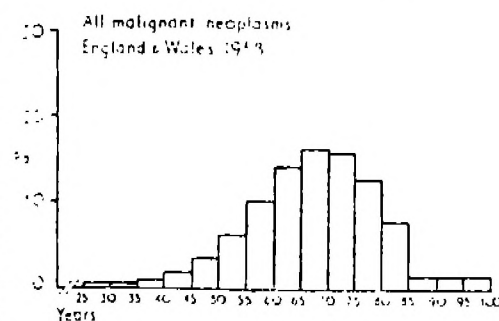
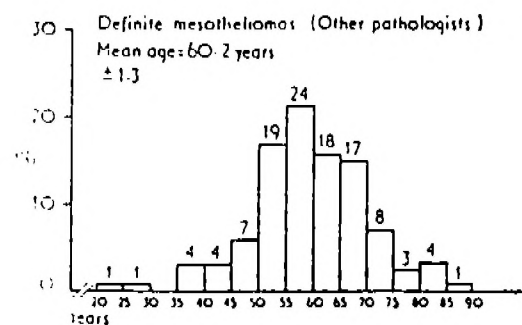
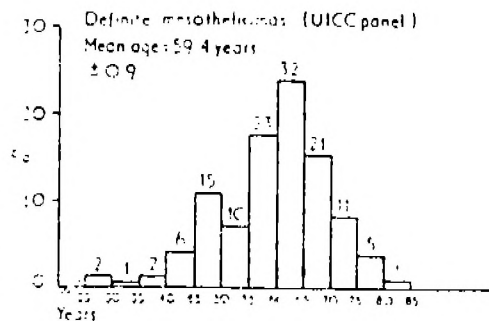


FIG. 1. Age distributions at death.

underdiagnosis in areas without large-scale asbestos industry, or to bias on the part of the interviewers who might have been more assiduous in pursuing an asbestos association history in cases of definitive mesothelioma. Ideally it would have been desirable to conceal from interviewers the diagnosis in individual cases, but on account of limited manpower the interviewer may have been responsible for identifying cases and arranging for confirmation of diagnosis. On the other hand, the number of notifications which were not subsequently fully confirmed but had

TABLE 5
INDUSTRY OR JOB FIELD IN 167 'DEFINITE'
MESOTHELIOMAS WITH DEFINITE OCCUPATIONAL
EXPOSURE TO ASBESTOS

Industry or job	Number of mesotheliomas
Shipworker	75
Asbestos factory worker	39
<u>Insulation worker (not marine)</u>	<u>13</u>
<u>Boiler house worker (not marine)</u>	<u>5</u>
Chemical worker	5
Docker	4
Welding rod manufacture	4
Building worker	3
Electrician	3
Sack cleaner/repairer	3
Welder/plater	3
Battery box manufacture	2
Electricity generating industry	2
Gas worker	2
Railway coach locomotive builder	2
<u>Motor mechanic</u>	<u>1</u>
Refuse work	1

known asbestos exposure may have been the result of over-diagnosis because of the well-known association of mesothelioma with this occupational history thus introducing a bias in the opposite direction.

The individual occupations of confirmed cases with industrial exposure are shown in Table 5. The degree of risk associated with these occupations cannot be computed because the population exposed, over a period of 50 years, is unknown and cannot even be guessed.

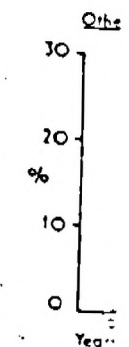
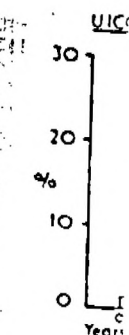
Table 6 lists those subjects with mesothelioma where a history of exposure to asbestos, not occupational in origin, was obtained. Of those subjects with neighbourhood exposure, the first four lived near the same asbestos factory in a district where chest physicians have a high awareness of mesothelioma. The final four subjects listed had exposures that might be considered minimal and common experience.

In cases notified to the register by the Registrar General for England and Wales a control group was established (from 1 January 1968), the next death registration matched for age and sex but not for area being notified to the register for comparison of occupation. It was found, however, that as cases of mesothelioma were more commonly referred to coroners than were other subjects the job description was frequently qualified to indicate asbestos exposure; for example, 'plumber' or 'fitter' was further categorized as 'shipyard', whereas no such qualification appeared in the controls. Even 'housewife' and 'widow' were recorded as occupations with the disease attributed to asbestos exposure.

Ethical considerations prevented the interviewing of control subjects (or their relatives) though it is

TABLE 6
NON-OCCUPATIONAL ASBESTOS EXPOSURE HISTORIES OBTAINED IN CASES OF MESOTHELIOMA

Case number	Duration of exposure	Nature of exposure
EW 67-70	25 years	Resident within yards of an asbestos factory; at school nearby
EW 68-174	14 years	Resident close to an asbestos factory; probably went to school nearby; both parents worked in asbestos factory
EW 68-38	3 years	Worked next door to asbestos factory
	22 years	Resident 1½ miles from same asbestos factory
EW 68-86	Unknown	Hobby: relining and refitting clutches and brakes
S 68-71	15 years	Resident 200 yards from an asbestos factory
S 68-31	30 years	Resident < ¼ mile from a shipyard
S 68-23	Unknown	Resident < ¼ mile from a shipyard
EW 67-82	14 years	Resident ½ mile from an asbestos using factory
EW 67-115	Unknown	Resident < ¼ mile from an asbestos factory
EW 68-19	17 years	Resident < 1 mile from asbestos factory
	40 years	Resident < 1 mile from an asbestos factory
EW 68-88	2 years	Husband worked in an asbestos factory
EW 68-190	Unknown	Lived in a house largely composed of asbestos cement sheeting
	4 years	Worked on and lived adjacent to chicken farm composed of asbestos cement buildings
EW 68-186	3 years	Intermittent exposure to brother's overalls contaminated with asbestos
<u>EW 68-80</u>	<u>1 day</u>	<u>Sawing up asbestos cement sheets to construct two sheds</u>



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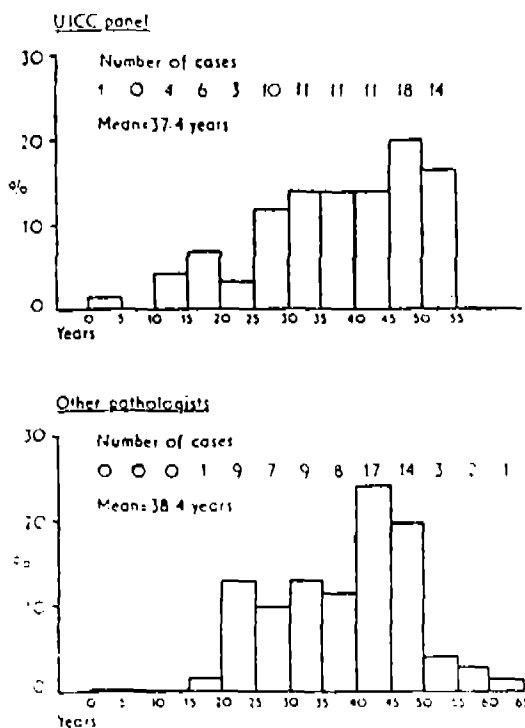


FIG. 2. Definite mesotheliomas with definite occupational asbestos exposure: survival after first exposure.

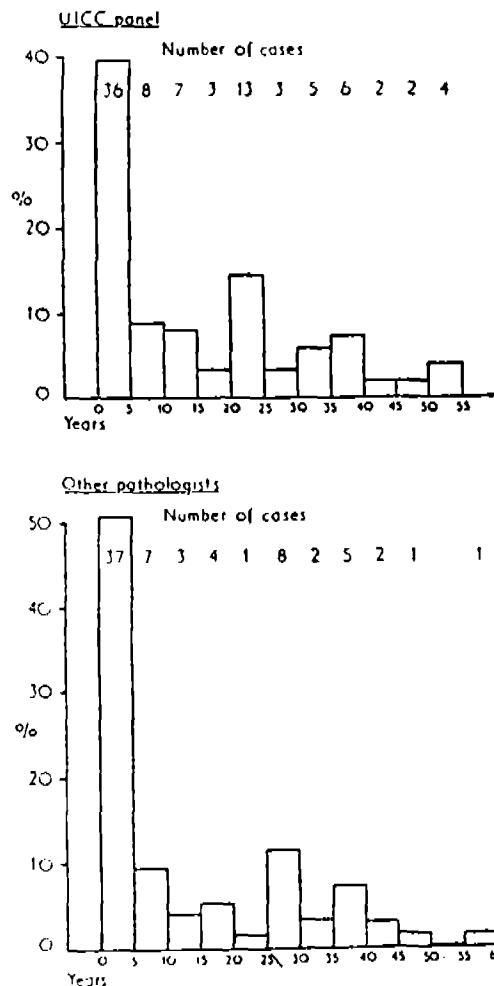


FIG. 3. Definite mesotheliomas with definite occupational asbestos exposure: survival after last exposure.

recognized that this would have been desirable (McEwen, Finlayson, Mair, and Gibson, 1970).

Figures 2, 3 and 4 illustrate time relationships with known asbestos exposure. In 85% of cases death occurred more than 25 years after first exposure, although the shortest period was three and a half years and the longest 53 years. There was no significant difference in the distributions of years of

TABLE 7

TYPE OF ASBESTOS INVOLVED IN OCCUPATIONAL ASBESTOS EXPOSURE

Asbestos type to which exposed occupationally	Histological diagnosis		
	Definite mesothelioma	Undecided and insufficient material	Definitely not mesothelioma
Chrysotile only	4	1	1
Crocidolite only	4	0	1
Amosite only	0	0	1
Chrysotile and other asbestos	42	8	7
Mixed asbestos without crocidolite	0	2	2
Type not ascertainable	117	25	15
Total	167	36	27

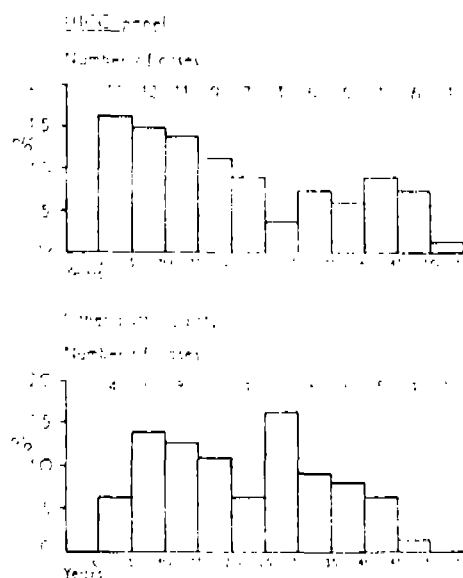


FIG. 4. Definite pleural mesothelioma: duration of occupational exposure to asbestos.

survival after first exposure in the two groups (mean age: UICC, 37.4 years; other pathologists, 38.4 years). The interval between last handling asbestos and death was under one year in about 40% cases but varied up to 52 years (one case). The duration of exposure was more widely spread, ranging from three weeks to over 50 years. Twelve per cent of cases had been exposed for under five years. The man with only three weeks' exposure died over half a century later.

Table 7 summarizes information regarding the type of asbestos, but this could be obtained in only a

small proportion of subjects. Of the 50 subjects with 'definite mesotheliomas', where the types of asbestos to which they were exposed were known, 45 had been exposed to crocidolite. Of the group of 12 subjects diagnosed as 'definitely not mesothelioma' in which types of asbestos to which they had been exposed were known, eight had been exposed to crocidolite.

There is no significant difference between these two groups. In four cases of definite mesothelioma no exposure was known other than to chrysotile. A history of exposure to talc was obtained in seven subjects with definite mesotheliomas, but six of them had also been exposed to asbestos. It was not possible to identify the nature of the talc to which they had been exposed.

Other evidence of asbestos exposure

It is apparent that a history of occupational exposure to asbestos is frequently associated with the presence of asbestosis, asbestos fibre bodies, asbestos fibres or pleural plaques observed at necropsy or radiologically (Table 8). Ashcroft and Heppleston (1973) stress the importance of phase contrast microscopy and electron microscopy in searching for asbestos in tissues. The presence of pleural plaques does not always indicate asbestos exposure (Rous and Studeny, 1970). It is not possible, however, to observe a significant difference of asbestos exposure between subjects with definite pleural mesotheliomas and those subsequently categorized as definitely not pleural mesothelioma.

In four 'definite pleural mesotheliomas' corroborative evidence of asbestos exposure was found in the absence of occupational exposure histories. Of those subjected to 'hobby' or 'domestic' exposure (six cases) none showed corroborative features. Of those with 'neighbourhood' exposure (eight cases), two had asbestos bodies.

TABLE 8
CORROBORATIVE EVIDENCE OF ASBESTOS EXPOSURE¹ RELATED TO OCCUPATIONAL EXPOSURE HISTORY AND NOTIFICATIONS TO MESOTHELIOMA REGISTER (PLEURAL TUMOURS ONLY)

Occupational asbestos exposure history	Definite pleural mesothelioma			Definitely not pleural mesothelioma		
	Corroborative evidence	No corroborative evidence	Not reported	Corroborative evidence	No corroborative evidence	Not reported
Definite	100 (69%)	24 (16%)	22 (15%)	19 (73%)	3 (12%)	4 (15%)
Possible	8 (50%)	4 (25%)	4 (25%)	0 (—)	3 (60%)	2 (40%)
None ascertainable	4 (13%)	18 (56%)	10 (31%)	0 (—)	6 (33%)	12 (67%)

¹Asbestosis, asbestos bodies, asbestos fibres or pleural plaques

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TABLE 9 (b)
GEOGRAPHICAL DISTRIBUTION OF MESOTHELIOMAS ASSOCIATED WITH OCCUPATIONAL ASBESTOS
EXPOSURE AND THE PROPORTION OF THESE CASES TO ALL CASES OF MESOTHELIOMA

Region ¹	Mesotheliomas with definite occupational asbestos exposure	
	No.	Percentage of all mesotheliomas
Greater London	29	50
Rest of SE England	12	67
SE Lancashire conurbation	13	81
Merseyside conurbation	22	88
Rest of NW England	8	100
Tyneside	8	89
Rest of N England	6	67
W Yorkshire conurbation	11	92
Rest of Yorks & Humberside	2	67
N Wales	1	33
SE Wales	6	60
E Anglia	—	—
Clydeside ²	22	79
Rest of Scotland	3	50
SW England	18	82
E Midlands	1	33
W Midlands conurbation	4	67
Rest of W Midlands	1	17
England, Wales & Scotland	167	68

¹Standard regions of Registrar General England & Wales, except Clydeside

²Dunbartonshire, Renfrewshire, Greenock, Glasgow, Hamilton, Motherwell

carcinoma, can produce widespread sheet-like growth resembling late diffuse pleural mesothelioma. Histologically the cellular and intercellular characteristics can be highly equivocal. The UICC pathologists' panel criteria for reaching a decision were modified in the course of the survey (see Appendix) and have not finally been decided (McCaughy and Oldham, 1974).

Willis (1952) cautioned against accepting the diagnosis of mesothelioma until, by careful search, an alternative primary neoplasm had been excluded. In a series of 3 771 necropsies Cameron, Litton, and Lyon (1961) found a prevalence of primary carcinoma multiplex of 1.2%. In the present series there were three with additional primary neoplasms in the 246 'definite' cases (one with carcinoma of the stomach, another with carcinoma of the bronchus, and the third with myelogenous leukaemia). This represents a prevalence of carcinoma multiplex of 1.2%. Sections referred to the UICC pathologists had previously been studied by other pathologists who had not necessarily made a diagnosis of mesothe-

lioma. In 182 cases where adequate histological material had been studied by UICC pathologists they made a diagnosis of mesothelioma in 134 (74%), were undecided in 10%, and made an alternative diagnosis on 30 occasions (16%). The concordance of diagnosis between UICC and other pathologists is greater in view of the fact that a number of sections were referred to the UICC panelists for a second opinion when the other pathologists had said the condition was not mesothelioma but an asbestos occupation history had been obtained by the clinicians.

In those cases with adequate histological material, not referred to the UICC panel (186 cases), a pathological diagnosis of definite mesothelioma was made in 112 (60%).

The submission of sections to the UICC panel varied in different parts of the country. In Greater London 77 out of 111 cases were referred (69% compared with only 12 out of 61 cases in Scotland (20%).

The number of cases diagnosed is unlikely to be

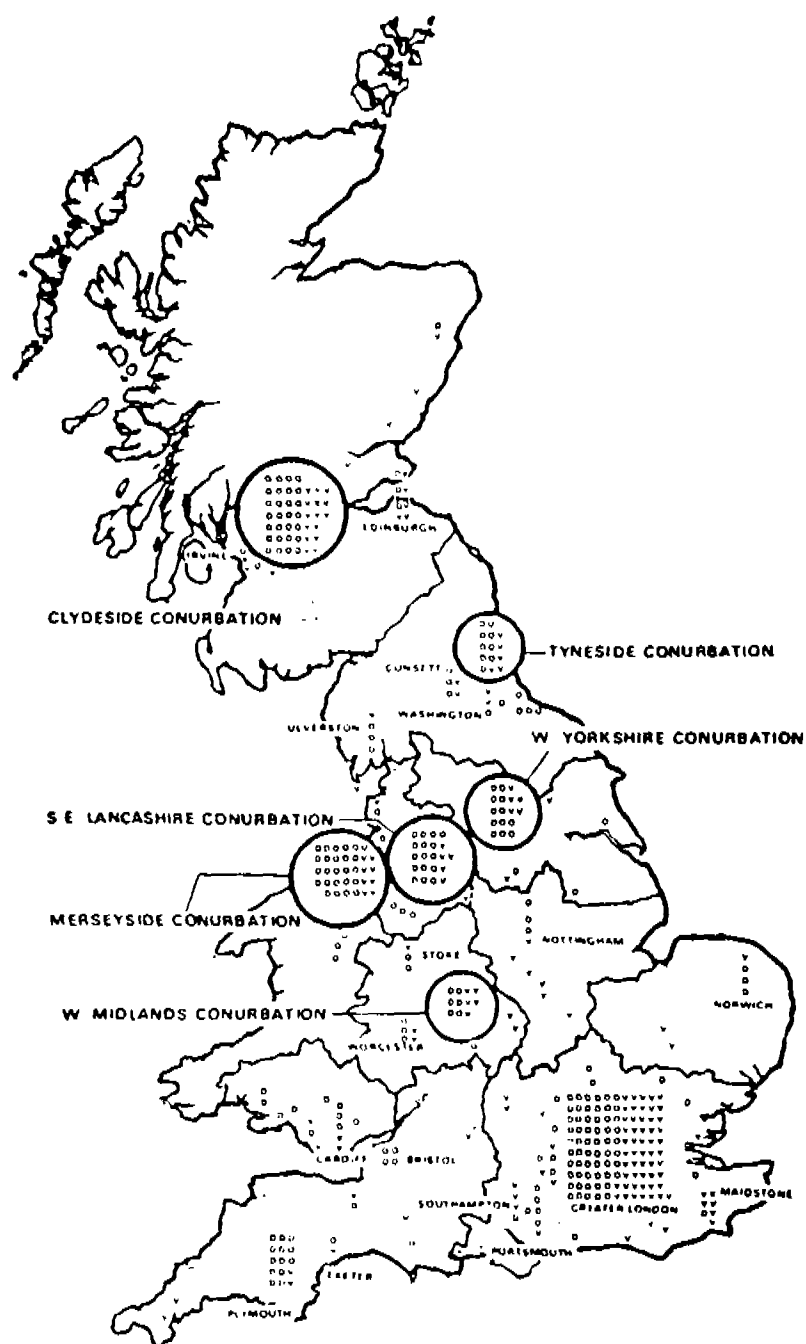


FIG. 5. Geographical distribution of notifications and confirmations of mesothelioma 1967-68 (standard regions employed by Registrar General except Clydeside which includes Dunbartonshire, Renfrewshire, Greenock, Glasgow, Hamilton and Motherwell): D = definite mesothelioma—UICC Panel; O = definite mesothelioma—other pathologists; V = other diagnoses.

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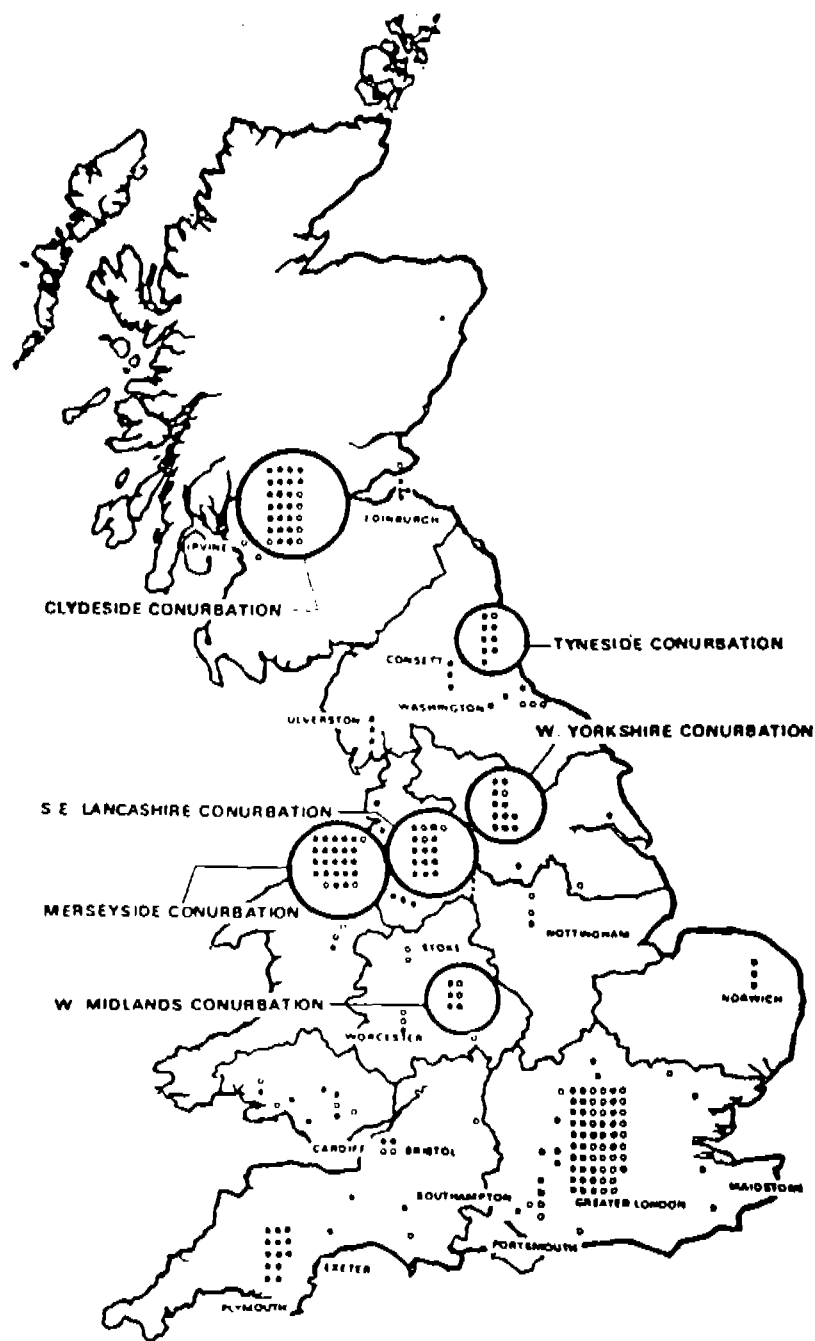


FIG. 6. Geographical distribution of definite mesotheliomas and associated occupational asbestos exposure; D = definite mesothelioma—UICC Panel; O = definite mesothelioma—other pathologists; ● = definite occupational exposure.

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APPENDIX

The UICC Panel of Pathologists and diagnostic criteria

A British panel of pathologists specializing in the diagnosis of mesothelial tumours was formed unofficially in 1963 and consisted of Dr. K. F. W. Hinson, Dr. E. Whitwell, Professor W. F. E. McCaughey, and Dr. J. C. Wagner.

From 1963 to 1967 all cases were examined by all members of the panel and a majority opinion was arrived at. Subsequently the panel was constituted as a UICC panel. From 1967 panellists decided whether the diagnosis was definitely mesothelioma, definitely not mesothelioma or whether there was insufficient histological material, only referring material to another member or members of the panel in case of doubt. After mid-1968 the policy was adopted that all cases referred to the panel should be seen by at least two members and that if there was a difference of opinion a third opinion should be sought. In mid-1971 the following protocol was designed for combined panel diagnosis. Two opinions are necessary for diagnosis and these two opinions should be combined as below:

		Second opinion			
		Definite	Probable	Possible	Not
First opinion	Definite mesothelioma	Definite	Definite	—	—
	Probable mesothelioma	Definite	Undecided	Undecided	—
	Possible mesothelioma	—	Undecided	Undecided	Not
	Not a mesothelioma	—	—	Not	Not

If the two opinions lead to a blank entry above then the specimen should be sent to the two other readers and a combined diagnosis made on the basis of four readings. There are many possibilities from four readings but the combined diagnosis should follow the majority if there is a clear one and otherwise be undecided. The following rule is sufficient to determine all cases of four readings: score a definite as 1 point, probable as $\frac{1}{2}$, possible as 0, not as -1; then add up the four scores and if the total is greater than or equal to $1\frac{1}{2}$ the diagnosis is Definite, between -1 and +1 inclusive it is Undecided, less than or equal to -1 is Not a mesothelioma.

Addendum

The Mesothelioma Register, which in 1967 and 1968 recorded cases from all available sources, has since continued with notifications of deceased cases only. The following table gives details of notifications (subject to confirmation) for the years up to 1971, figures for the years 1967 and 1968 being included on a similar basis for comparison.

NOTIFICATIONS TO THE MESOTHELIOMA REGISTER (DEATH CASES) 1967-71

Sources of notification	1967	1968	1969	1970	1971
Death certificate	91	189	126	165	124
Cancer Registry ¹	39	28	20	11	11
Industrial injury data ²	3	3	6	3	—
Other	20	13	5	5	3
Total	163	233	157	184	138

¹Not so certified at death

²Not on death certificate or cancer registration

In the short period studied it is not possible to observe a significant trend. The large number of cases notified in 1968 may have resulted from the publicity and vigilance generated by the survey. If the impression of a falling off in notifications is confirmed then whether this will be due to a change in the prevalence of the disease or to a change in vigilance will require to be evaluated.

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