Papers and Originals

Mesothelioma in Scotland

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Summary: In a retrospective study of the incidence of mesothelioma in Scotland for 1950-67 80 cases were traced from pathological reports and biopsy material of malignant tumours invading the pleura and peritoneum. These cases were matched with two sets of controls. Detailed histories of residence, occupation, and degree of exposure to asbestos confirmed that the incidence of mesothelioma in Scotland is similar to that in other parts of Britain.

Introduction

An association between exposure to asbestos and subsequent development of malignant mesothelioma of the pleura was reported by Wagner *et al.* (1960) in South Africa. The results of several epidemiological studies of mesothelioma (First International Conference on the Biological Effects of Asbestos, 1965) confirmed the association between mesothelioma and previous exposure to asbestos dust. By 1965 160 cases of mesothelioma had been recorded in the United Kingdom, of which 123 were from England and Wales, 36 from Northern Ireland, but only one from Scotland (Gilson, 1966). A further five cases were reported in Glasgow (Gold and Cuthbert, 1966).

Further studies of mesothelioma, as well as the more general aspects of asbestos and health, have been reported (Second International Conference on the Biological Effects of Asbestos, 1968; Department of Mines, Republic of South Africa, 1969). Wright (1969) has also surveyed the present state of knowledge about asbestos, with particular reference to American experience.

It seemed unlikely that the real incidence of mesothelioma in Scotland could differ substantially from that in other areas in the United Kingdom. In particular, many of the cases in Belfast (Elmes *et al.*, 1965) had been associated with asbestos in shipbuilding or ship-repairing. Since Clydeside employs about twice as many men in these industries as Belfast (*Shipbuilding Inquiry Committee*, 1966) more cases could probably be found in this area.

From a preliminary investigation of the records of the Registrar General for Scotland a total of 22 deaths from mesothelioma for the years 1953-65 were found. Since death certificates alone are unlikely to reflect the true incidence of such a rare tumour a more detailed survey was needed, based on pathological material (Heasman and Lipworth, 1966; Newhouse and Wagner, 1969). This paper describes a retrospective survey of cases of mesothelioma in Scotland during 1950-67 and reports the results of a controlled epidemiological study of these cases.

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Methods

The study was carried out in two parts: identification and collection of all cases of malignant mesothelioma, and a comparison of these cases with two sets of controls in respect of history of exposure to asbestos dust.

Identification

Necropsy and surgical biopsy reports in all university and hospital pathological departments in Scotland were reviewed by one of us (A.A.M.G.) for the years 1950-67, the only exceptions being two hospitals where studies of mesothelioma were already in progress. These two hospitals have, however, allowed their cases to be included in the epidemiology study. Records for the five years preceding 1950 were also examined where available, but no cases were found for that period.

The method of screening the pathological reports and material was the same in each department. All necropsy reports of malignant tumour affecting the pleura or the peritoneum were reviewed and the cases of metastatic tumour with an obvious primary lesion were not examined further. Where the site of the primary tumour was doubted, or where the diagnosis of peripheral bronchial carcinoma had been made, the tumour was examined microscopically, with the exception of unequivocal cases of squamous carcinoma. Most cases examined microscopically were excluded because they had the histological pattern of a mucin-secreting adenocarcinoma or of an adenocarcinoma lacking distinguishing features. If the histological patterns were characteristic of mesothelioma, such as tubulo-papillary architecture with uniform cubical tumour cells or a non-specific structure such as spindle-cell sarcoma or anaplastic malignant tumour, if there was diffuse neoplastic growth in the pleural cavity or peritoneum, and if all other sources of primary malignancy had been excluded the diagnosis of diffuse mesothelioma was made.

In cases where the diagnosis was based on biopsy material the same histological criteria were applied, but the clinical and radiological findings or the results of special investigations such as the cytology of pleural fluid, bronchoscopy, or thoracotomy were taken into account.

These pathological criteria follow closely the recommendations of the International Union Against Cancer, 1965.

Selection of Controls

Two sets of controls were selected. One of these represented as nearly as possible the baseline of exposure to asbestos in the general population—that is, patients whose death was attributed to a disease not thought to have any possible association with asbestos—coronary artery disease. The other set of controls represented a disease, carcinoma, in which there was already a known or suspected relationship with exposure to asbestos; patients who had died from lung and gastric carcinoma were matched with those with pleural

and peritoneal mesothelioma, respectively. In the latter group of controls it was expected that the degree of exposure to asbestos would probably lie between that of the cases of mesothelioma and the cardiovascular controls.

Each case of mesothelioma was matched with the nearest chronological entry in the necropsy records of the same hospital for patients dying of coronary artery disease and lung and gastric carcinoma. Controls were matched for age (plus or minus five years) and sex. Residence was not specifically controlled, since most hospitals tend to take patients from a restricted area, but subjects who might have been used as controls were excluded if their address was in a rural district or an island when the patient came from an urban area.

Cases and controls were compared for exposure to asbestos by detailed occupational and residential histories obtained from the next of kin or relatives (hereafter referred to collectively as relatives). With the co-operation of hospital medical superintendents, the names and addresses of relatives of both cases and controls were obtained from medical records departments, together with the names of the respective consultants and general practitioners. Letters were sent to the doctors concerned, explaining the purpose of the study and allowing them time to express objections to the study if they felt that the relatives might be upset, or to raise any query about the proposed visit to the relatives.

Letters were then sent to the relatives asking their permission to be interviewed. Apart from explaining that, as part of a research study into the relationship of health and occupation the department was collecting information on a number of persons who had died in Scotland between 1950 and 1967, the letters made no mention of the cause of death. A sociologist experienced in interviewing (A.F.) carried out all the visits. To avoid any possibility of prior knowledge of the medical history influencing the assessment of asbestos exposure, the interviewer did not know whether she was visiting the relatives of a case or of a control. A fuller description of the methods and the more general difficulties encountered in tracing and obtaining the co-operation of relatives will be published elsewhere.

Relatives were traced for all except two cases, and for each of these a neighbour was found who could give some basic information. One case was excluded because the relative refused to co-operate. No controls of matching age could be found in necropsy records for one case, and no cancer control for a further case. As three possible controls were rejected after extensive inquiries had yielded no informants at all, substitutes (the next suitable entries in necropsy records) were obtained for these three. Similarly, substitutes were obtained for five controls who were considered unsuitable on medical advice, for five whose relatives said they did not know enough about the subject, and for 13 where relatives refused to co-operate. Neighbours were accepted as informants for five controls where no relatives could be traced.

As obtaining interviews with relatives of controls was very difficult in a few instances, substitute controls were selected on identical criteria. The names of their relatives were inserted in the lists of later visits without any indication that they were substitutes. From the evidence available in hospital records there was no suggestion that possible controls who were discarded differed in occupational distribution from controls who were used.

Assessment of Exposure to Asbestos

Occupational Exposure.—Most relatives were able to provide fairly comprehensive occupational histories with considerably more detail than was generally available from hospital reports. The information was classified as follows:

Definite.—Direct information obtained from relatives that the subject had worked with asbestos. Very seldom was the type of asbestos known.

Probable.—Relatives were not certain what substances the subject had used in his work, but his occupational history suggested to the interviewer that he was very likely to have used asbestos.

Possible.—Relatives were not certain what substances the subject had encountered, but his occupational history suggested to the interviewer that he was likely to have worked beside others using asbestos and might occasionally have used it himself.

None.—Relatives stated that the subject had not used asbestos and the occupational history was such that exposure to asbestos seemed unlikely.

Neighbourhood Exposure.—Relatives were asked whether any of their addresses were within half a mile (800 m.) of asbestos factories or asbestos dumps, shipyards, or docks, and this was subsequently checked on a map. Any such residence constituted neighbourhood exposure and the number of years was noted.

Domestic and Family Exposure.—Information was obtained as to whether the subject used asbestos in his spare time and whether members of his household worked in industries or occupations at risk.

Smoking Habits.—The association between smoking and the development of lung carcinoma and coronary artery disease (the two control groups) is well known. In a report emphasizing the importance of smoking, when combined with exposure to asbestos, in the development of lung cancer, the calculations of Selikoff *et al.* (1968) suggested that asbestos workers who smoked had about 92 times the risk of dying of bronchial carcinoma as men who neither worked with asbestos nor smoked. The smoking habits of the cases of mesothelioma and of the controls were therefore compared.

Results

The diagnosis of mesothelioma was accepted in 83 cases in Scotland for the years 1950-67. Of these, two normally lived in England and so were excluded, and the relatives of one refused to co-operate. Thus 80 cases (73 men and 7 women) were available for epidemiological study (Table I, Fig. 1). The sites of the tumours are shown in Table II. In 19 cases of pleural tumour the diagnosis was based on a biopsy; the

TABLE I.—*Mesothelioma in Scotland. Year of Diagnosis of* 80 *Cases*

1950	1	1953	3	1956	0	1959	1	1962	4	1965	11
1951	1	1954	1	1957	0	1960	8	1963	4	1966	9
1952	1	1955	1	1958	2	1961	2	1964	11	1967	20

TABLE II.—*Site of Tumour*

	Pleural	Peritoneal	Both
Men	69	2	2
Women	6	1	0

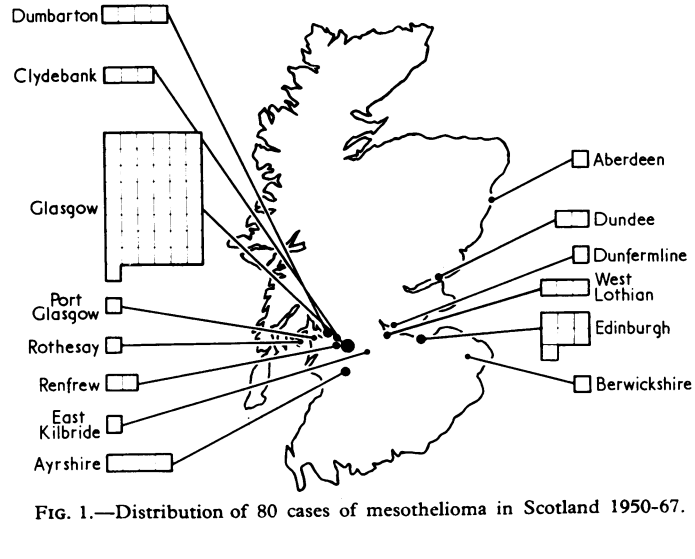

FIG. 1.—Distribution of 80 cases of mesothelioma in Scotland 1950-67.

TABLE III.—*Age Distribution of Cases*

Age:	<40	40–49	50–59	60–69	70–79	80+	Total
No. of cases Male	5	7	23	25	9	4	73
No. of cases Female	0	0	2	3	2	0	7

TABLE IV.—*Smoking Habits (Males)*

M.R.C. Category	Cases of Mesothelioma	Controls	
		Carcinoma	Cardiovascular
1. Non-smokers	12 (16%)	4 (6%)	4 (6%)
2 and 3. 1-14 g./day	30 (41%)	16 (23%)	21 (29%)
4. 15-24 „	18 (25%)	25 (35%)	22 (31%)
5. 25+ „	12 (16%)	25 (35%)	21 (29%)
Incomplete information	1 (1%)	1 (1%)	4 (6%)

TABLE V.—*Residential Exposure (Males)*

	Cases of Mesothelioma	Controls		Total
		Carcinoma	Cardiovascular	
No	22	34	37	93
Yes	51	37	35	123
Total	73	71	72	216

TABLE VI.—*Comparisons of Occupations (Males)*

	Cases of Mesothelioma	Controls	
		Carcinoma	Cardiovascular
Ever employed in shipbuilding, seagoing, docks (classes III, IV and V)	49 (67%)	23 (32%)	22 (31%)
Ever employed in other heavy industries (classes III, IV and V)	48 (66%)	51 (72%)	48 (67%)

TABLE VII.—*Detailed Breakdown of "Shipbuilding, Seagoing, Docks" Occupational Group*

Shipyard Workers	Cases of Mesothelioma	Controls	
		Carcinoma	Cardiovascular
Engineers, semiskilled and unskilled engineering labourers	32	15	12
Painters, red leaders, caulkers	3	5	2
Plumbers	5	—	1
Insulators	1	—	—
Electricians	3	1	1
Joiners	2	—	1
Watchmen, etc.	—	2	3
Dockers	2	(1)	2
Navy and Merchant Navy	1+(6)	(1)	(3)

Figures in parentheses represent men who were also employed in the shipyards at some time.

TABLE VIII.—*Definite Exposure to Asbestos*

	Cases	Controls
Shipyards:		
Plumbers	3	
Joiners	2	
Electricians	1	
Welder and Boiler-maker	1	1
Metal Worker	1	
Pipe coverer	1	
Unskilled and semiskilled labourers	3	
Other trades:		
Dock labourer	1	
Insulating engineers	4	
Asbestos cement worker	1	
Rubber factory worker	1	
Building trade labourer	1	1

remaining cases in the series were diagnosed from necropsy evidence. The age of the patients at death ranged from 28 to 87 (Table III).

Because of the small number of women, comparisons have been made only between the 73 men and their controls.

Smoking.—The categories were defined by the Medical Research Council (1966a, 1966b) (Table IV). When all the M.R.C. categories are compared the difference is significant at the 1% level (Table IV).

Exposure to Asbestos.—Significantly more cases than either of the two control groups had lived within half a mile (800 m.) of shipbuilding, docks, or asbestos factories, and most of them had spent more than 30 years of their lives in these areas (Table V). Of the 51 male cases who had residential exposure, all but one also had some evidence of occupational exposure to asbestos. None of the five female cases with residential exposure had occupational exposure.

Domestic Exposure.—Only a few of the men had used asbestos in connexion with their hobbies or spare-time activities. Similarly, only a few of the cases and controls had relatives who were known to have worked with asbestos. There was no statistical difference with regard to either household or spare-time exposure to asbestos between the three groups.

Occupational Exposure.—Subjects were classified according to whether they had ever worked in certain occupations, as follows:

Occupational Group	Degree of Skill	Registrar General Social Classes
All non-manual occupations		I, II, III (non-manual)
Shipbuilding, docks, seagoing	Skilled	III
	Semiskilled and unskilled	IV and V
Other heavy industries	Skilled	III
	Semiskilled and unskilled	IV and V
All other occupations	Skilled	III
	Semiskilled and unskilled	IV and V

Two of these occupational groups were selected for comparison (Table VI). A significantly higher proportion of cases had worked at some time in the shipbuilding industry, docks, or seagoing occupations compared with controls ($\chi^2=23{\cdot}1$ with 2 degrees of freedom; $P<0{\cdot}005$). There is no difference between cases and controls in other heavy industries ($\chi^2=0{\cdot}4$ with 2 degrees of freedom; $P>0{\cdot}75$) nor between the skilled and unskilled categories. Within the shipbuilding industry cases and controls were distributed in similar proportions throughout the various trades (Table VII).

When all categories of occupational exposure to asbestos are considered there is a highly significant difference between cases and controls ($\chi^2=84{\cdot}0$ with 6 degrees of freedom; $P<0{\cdot}005$) (Fig. 2). On the other hand, in the category of

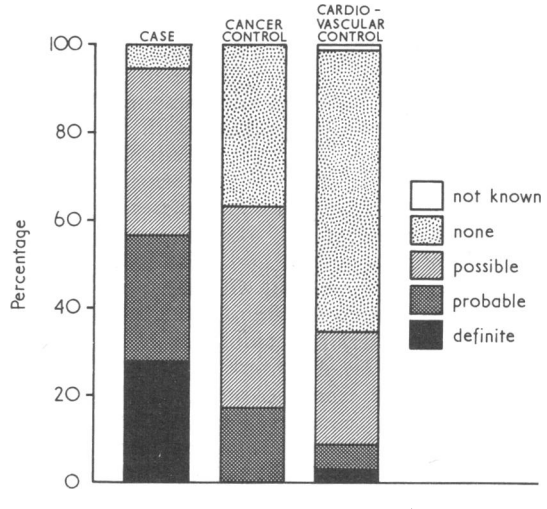

FIG. 2.—Mesothelioma and occupational exposure to asbestos.

"definite" exposure to asbestos 20 cases, no cancer controls, and two cardiovascular controls were exposed to asbestos, and this is also highly significant ($\chi^2=36{\cdot}0$ with 2 degrees of freedom; $P<0{\cdot}005$). If the lung cancer controls are compared with the cases of mesothelioma and then with the cardiovascular controls they are seen to be significantly different from both in respect of exposure to asbestos. (Lung cancer controls and mesothelioma cases: $\chi^2=38{\cdot}976$, $P<0{\cdot}005$; and lung cancer controls and cardiovascular controls: $\chi^2=11{\cdot}79$,

$P<0.005$.) More than half of the subjects had been exposed to asbestos during their work in the shipyards in a wide variety of trades (Table VIII). Insulating engineers form the next largest group, and at times they were employed in the shipyards.

Discussion

At the beginning of this study only a few cases of mesothelioma in Scotland had been reported. As the study progressed, additional cases came to light, particularly in the later years of the survey.

Of the 22 cases noted in the records of the Registrar General for Scotland for the years 1955-63, only nine were included in the present series. A further 41 cases which had not been recorded by the Registrar General for the years 1955-63 were also included. Of these, 34 were traced by a detailed search of the records of the Registrar General for Scotland, and the diagnoses at death are as follows: pleural effusion 4; lung cancer 21; carcinomatosis 2; pleural tumours 5; others 2. Of the five recorded as pleural tumours three were mesotheliomas, one was pleural endothelioma, and one was fibrosarcoma of pleura. These did not appear when the records of the Registrar General were originally checked in an attempt to find mesotheliomas.

Only cases of mesothelioma which had been admitted to hospital and in which there was histological evidence to support the diagnosis are described in this study. The greater awareness in recent years of the link between asbestos and malignancy may have accounted for more patients with chest conditions and a history of occupational exposure to asbestos being admitted to hospital for full investigation. Since mesothelioma became a prescribed disease in 1966, relatives may possibly have been more willing for necropsy examinations to be carried out to establish a diagnosis. As the diagnosis of mesothelioma in this series is based on a review of hospital records and pathological material, the rise is unlikely to be attributable to a change in diagnostic practice, though undoubtedly the diagnosis has become more acceptable recently. Nevertheless, there seems to have been a genuine increase in cases of mesothelioma occurring in Scotland, and this accords with similar increases reported in other published series and also with the greater use of asbestos in industry.

Our analysis of occupational exposure to asbestos shows a very significant difference between the mesothelioma cases and both sets of controls, both when definite exposure is considered alone and when all grades (definite, probable, and possible) are considered. The lung cancer controls would be expected to fall about midway between the mesothelioma cases and the cardiovascular controls, and this in fact occurred. When occupations are grouped according to industry, significantly more men with mesothelioma had been employed at some time in the shipbuilding industry compared with the controls; this was not confined to any one trade within the industry (Table VII). Exposure to asbestos occurred in a wide variety of trades, and indicates that the total working environment should be considered rather than just the actual trade in checking for exposure to possible hazards. Apart from those employed as insulators, only one case had been associated with manufacturing an asbestos product, and this probably reflects both the small number of people employed in asbestos manufacturing in Scotland and the success of measures taken to suppress asbestos dust in this industry.

In only one case and one control was there evidence of definite exposure to asbestos in the building trade. This figure is lower than would be expected from the amount of asbestos used, particularly in the more modern buildings; however, the asbestos content of materials used in building may be less well known to users than is the asbestos content of insulating materials used in shipyards. In both shipbuilding and other industries, mobility of labour was high, especially in the depression and war years; thus the distribution of domiciles at death (Fig. 2) does not provide a complete geographical representation of occupational exposure to asbestos.

Evidence of asbestosis was found only in two of the cases of mesotheliomas. Thus the level of exposure to asbestos dust may be lower or more intermittent than in other series. An attempt was made to assess the length of exposure, the time of first exposure, and the latent period between exposure and development of mesothelioma. In this type of retrospective study, however, it was not possible to obtain accurately the exact times that a person had worked with asbestos, even when the relatives were certain that he had used it; nor was it possible to obtain from relatives information about the type of asbestos.

This study has shown that the incidence of mesothelioma in Scotland is similar to that in other parts of the United Kingdom (Elmes *et al.*, 1965; Newhouse and Thompson, 1965), and the association between the development of the tumour and occupational exposure to asbestos has been confirmed.

We would like to thank the many consultant pathologists and their staff, the hospital consultants and general practitioners, the hospital medical records officers, and many others throughout Scotland who, by their help and co-operation, have enabled this study to be carried out. We would also like to thank the Medical Research Council for financial support; Dr. J. C. Gilson, of the Pneumoconiosis Research Unit for advice; and Mr. J. Pearson, of the Department of Social and Occupational Medicine, University of Dundee, for statistical advice and help. Finally, we acknowledge our indebtedness to the many relatives who so willingly provided the necessary information and made this study possible.

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