

Pleuropneumonectomy in the management of diffuse malignant mesothelioma of the pleura

Experience with 29 patients

E. G. BUTCHART, T. ASHCROFT¹, W. C. BARNESLEY,
and M. P. HOLDEN

Department of Cardiothoracic Surgery, Shotley Bridge General Hospital and Department of Pathology, University of Newcastle upon Tyne

Butchart, E. G., Ashcroft, T., Barnesley, W. C., and Holden, M. P. (1976). Thorax, 31, 15–24. Pleuropneumonectomy in the management of diffuse malignant mesothelioma of the pleura. Experience with 29 patients. An analysis is made of the results of pleuropneumonectomy for diffuse malignant pleural mesothelioma in 29 patients and a comparison is made with the results of non-surgical treatment in a further 17 patients. A system of tumour staging is proposed, and the results are correlated with tumour stage and with histological type. Pleuropneumonectomy does not appear materially to affect the course of the disease in cases of mixed epithelial and mesenchymal histological type. However, stage I cases of pure epithelial histological type appear to carry a better prognosis, especially those whose histological structure consists entirely of abundant oedematous mucoid stroma with loosely arranged tumour cells. It is suggested therefore that only epithelial cases should be subjected to pleuropneumonectomy. Means of reducing operative mortality are discussed and alternative methods of treatment described.

Diffuse malignant mesothelioma of the pleura is a highly malignant tumour, the course of which averages nine months from diagnosis to death (Wagner, 1971) or 13 to 14 months from first symptom to death (Elmes, 1973a). Very few patients survive longer than two years irrespective of the treatment they receive. This has led to a conservative attitude to the management of mesothelioma, exemplified by a recent review of therapeutic alternatives (Elmes, 1973b) in which the conclusion was that all forms of treatment were valueless and that only symptomatic treatment was justified. In particular, reviewing surgically treated cases, Elmes could find no authenticated case of prolonged survival.

Asbestos exposure on Tyneside occurs in many industries, notably shipbuilding (Ashcroft, 1973), and our resulting experience with a relatively large series of patients with diffuse malignant mesothelioma leads us to dispute this conservative approach. A study of our surgical and pathological

experience enables us to make a reappraisal of the place of pleuropneumonectomy.

MATERIAL AND METHODS

SURGICAL PATIENTS Twenty-nine patients (20 men and 9 women) underwent pleuropneumonectomy between 1959 and 1972. The mean age at operation was 52.4 (range 35–63) years. Most patients gave a history of asbestos contact, often over more than 30 years before developing symptoms. The commonest presenting symptoms were pain and dyspnoea, sometimes associated with a feeling of heaviness on the affected side of the chest. Their chest radiographs showed either a pleural effusion or pleural thickening.

The time between onset of symptoms and operation averaged 9.5 months (range 2 months to 4 years).

In 17 patients, the disease involved the right pleura, and in 12 patients the left.

NON-SURGICAL PATIENTS Seventeen patients (16 men and 1 woman) received various combinations of medical treatment:

¹Present address: Department of Pathology Leighton Hospital, Crewe, Cheshire

Pleural aspiration only	6 patients
Intrapleural cytotoxic drugs	2 patients
Intrapleural radioactive gold	1 patient
Intrapleural cytotoxic drugs and radioactive gold	1 patient
Intrapleural cytotoxic drugs and radiotherapy	1 patient
No record of treatment given	6 patients

Because of incomplete records and the small numbers of cases involved, no attempt has been made to assess the results of any specific form of treatment. Instead, they have been used as a relatively homogeneous group of non-surgical cases for the purpose of comparison.

The mean age at onset of symptoms was 58.5 (range 47-73) years.

DIAGNOSIS In the surgical patients, the diagnosis was suggested by the combination of asbestos exposure and radiographic evidence of pleural pathology and in some cases confirmed by pleural fluid cytology and needle biopsy of the pleura. In many patients, however, the radiological appearance of the characteristic pleural thickening was regarded as sufficiently pathognomonic, and the diagnosis was confirmed at operation by frozen section histology.

All the non-surgical patients had the diagnosis confirmed at necropsy.

SURGICAL TECHNIQUE The surgical approach for all cases was a standard posterolateral thoracotomy through the bed of the excised 6th rib. Blunt dissection was begun extrapleurally, and the parietal pleura was stripped off the chest wall. From the apex, the mediastinal pleura was stripped down towards the hilum, taking the paratracheal nodes en bloc. The internal mammary vessels were ligated at the apex and inferiorly, and the lymph nodes in relation to these vessels were dissected off the chest wall with the pleura.

Anteriorly, the pericardium was opened and excised widely as it was frequently involved by direct extension of tumour.

Posteriorly, the extrapleural dissection was continued to the hilum, dissecting out subcarinal and paraoesophageal nodes. The pericardium was opened posteriorly over the left atrium.

Hilar structures were dealt with in a standard fashion as in any intrapericardial pneumonectomy. The diaphragm in most cases was completely excised, the tumour often being thickest at this point. In five cases with minimal diaphragmatic involvement, it was possible to develop a plane of dissection between the diaphragmatic muscle and the peritoneum, leaving the latter almost entirely intact.

The surgical specimen therefore consisted of pleura, lung, lymph nodes, ipsilateral pericardium, and diaphragm. In 24 cases, it was necessary to reconstruct the diaphragm using industrial nylon or Dacron-reinforced Silastic¹ which was sutured to the chest wall or a rim of healthy diaphragm and the inferior pericardium with a continuous suture. In the remaining five cases, the diaphragmatic peritoneum was closed, producing a satisfactory barrier between the chest and abdomen.

In 15 cases, the pericardial defect was patched with nylon or Dacron-impregnated Silastic, and in the remaining 14 cases it was left open.

PATHOLOGY The histological diagnosis was reviewed and confirmed in all 46 cases by one of us (T.A.). The tumours were classified histologically into three types: pure epithelial, mixed epithelial and mesenchymal, and pure mesenchymal (Table I). The histological criteria were those generally accepted (McCaughy, 1958 and 1965; Hourihane, 1964; Ashcroft, 1973). We did not subdivide the epithelial group into an undifferentiated polygonal type and a tubopapillary type, as suggested by Whitwell and Rawcliffe (1971), because both these types occurred in combination in some cases.

TABLE I
HISTOLOGICAL CLASSIFICATION OF DIFFUSE
MALIGNANT MESOTHELIOMA

Histology	Surgical Patients	Non-surgical Patients	Total
Epithelial	11	7	18 (39.1%)
Mixed	17	7	24 (52.2%)
Mesenchymal	1	3	4 (8.7%)
Total	29	17	46

However, we were able to identify a histological variant within the epithelial group showing a distinctive histological structure, characterized by abundant oedematous mucoid stroma and relatively small numbers of loosely arranged tumour cells with poorly formed tubules, clefts, and sometimes cystic spaces (Figs. 1 to 3). This variant occurred in pure form in three patients and was classified as epithelial type A. Epithelial cases showing no evidence of these features were classified as epithelial type B, and those showing the features of type A in varying proportions with the more usual tubopapillary structure as type AB (Table II). The justification for this subclassification is its apparent prognostic significance, which is discussed below.

In addition, in order to facilitate analysis of the

¹Dow Corning Corporation, Midland, Michigan, USA, 48640

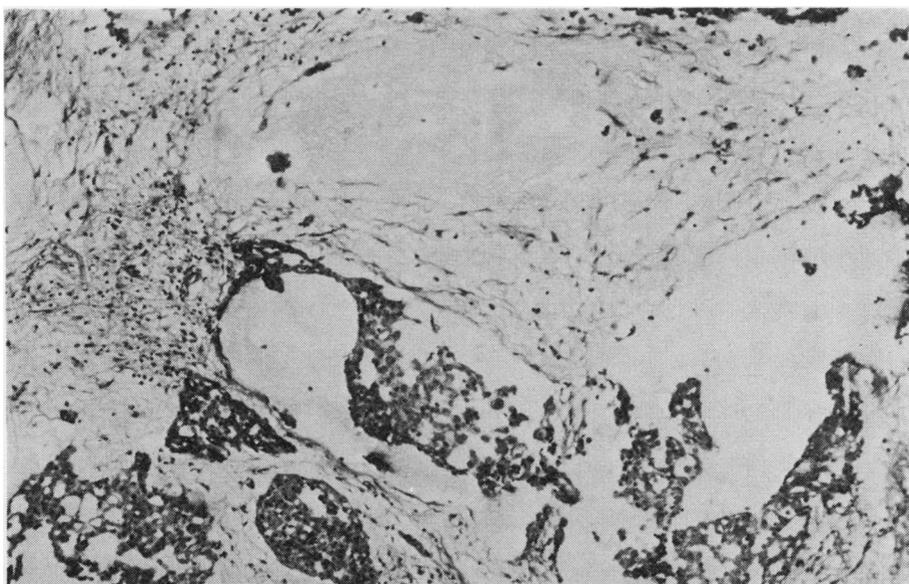


FIG. 1. *Case 11 (see Table VI). Shows oedematous mucoid stroma, separating irregular spaces which are partly filled with tumour cells (Haematoxylin and eosin $\times 85$).*

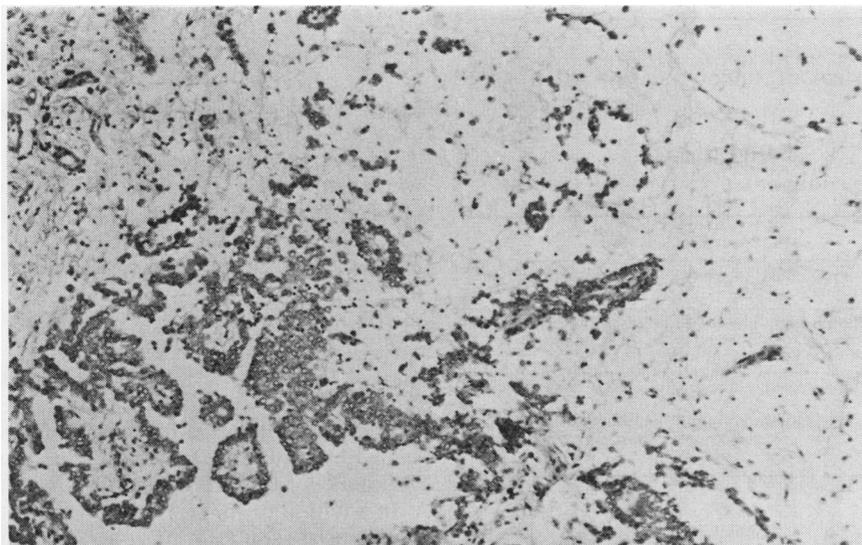


FIG. 2. *Case 2 (see Table VI). Shows similar tissue to Fig. 1 including poorly formed tubules (H and E $\times 85$).*

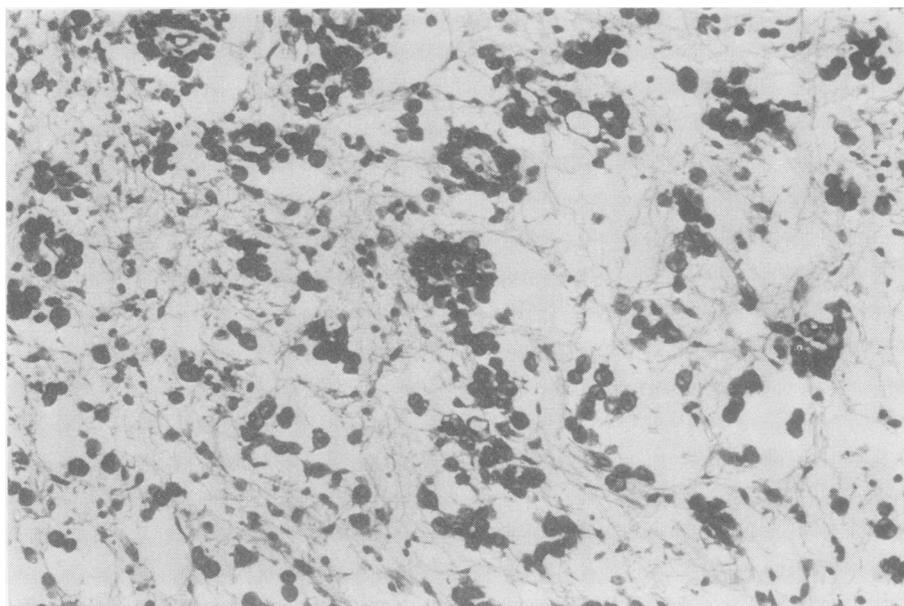


FIG. 3. Case 34 (see Table IX). Shows a region of oedematous variant in a tumour also containing other types (H and E $\times 180$).

TABLE II
SUBCLASSIFICATION OF THE EPITHELIAL GROUP

Type	Surgical Patients	Non-surgical Patients	Total
A	3	0	3 (16.7%)
AB	2	2	4 (22.2%)
B	6	5	11 (61.1%)
Total	11	7	18

results, a system of tumour staging is proposed (Table III).

TABLE III
CLINICOPATHOLOGICAL STAGING OF DIFFUSE MALIGNANT MESOTHELIOMA

Stage	Clinicopathological Staging
I	Tumour confined to homolateral pleura, lung, and pericardium
II	Tumour invading chest wall or involving mediastinal structures, eg, oesophagus, heart, opposite pleura Lymph node involvement within the chest
III	Tumour penetrating diaphragm to involve peritoneum directly Lymph node involvement outside the chest
IV	Distant blood-borne metastases

RESULTS

SURGICAL CASES The postoperative survival curve (Fig. 4) shows that the hospital mortality for the

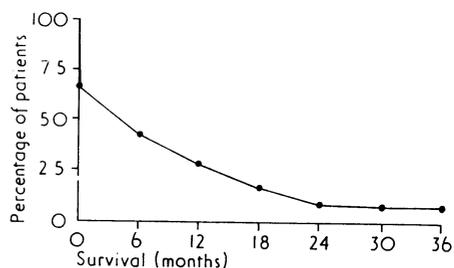


FIG. 4. Overall postoperative survival. The steep fall of the graph represents hospital mortality.

whole series was 31% and that only three patients (10.3%) survived two years or longer. However, two of these three patients are alive and well with no evidence of recurrence 3½ and 6 years respectively after operation.

Immediate results Hospital mortality showed a marked increase over the age of 60 years (Table IV). Analysis of the hospital mortality (Table V) revealed that seven of the nine deaths could have been prevented by better case selection, alteration in surgical technique, or better postoperative management.

In addition to the nine deaths, four other patients experienced significant postoperative complications: three patients suffered thromboembolic complications and one patient required reoperation for a

TABLE IV
HOSPITAL MORTALITY RELATED TO AGE

Age Group	No. of Cases	No. of Deaths	% Mortality
30-39	2	0	0
40-49	10	3	30
50-59	9	2	22.2
60-69	8	4	50

TABLE V
ANALYSIS OF HOSPITAL MORTALITY (9 CASES)

Theoretically preventable	Respiratory failure	3 cases
	Respiratory failure + bronchial fistula	1 case
	Pneumonia in remaining lung	1 case
	Pulmonary oedema following resuscitation from cardiac arrest due to massive haemorrhage	1 case
'Unpreventable'	Secondary haemorrhage into pneumonectomy space following anticoagulants	1 case
	Massive pulmonary embolism Myocardial infarction	1 case 1 case

chylothorax. The total complication rate was 44.8%.

In two patients dying from respiratory failure, complications related to the prosthetic diaphragm were contributory factors. In one patient, ineffective suturing of the prosthesis to the chest wall permitted the stomach to herniate into the pneumonectomy space posteriorly, necessitating reoperation. In another patient, a bronchial stump fistula developed during prolonged artificial ventilation, and air under tension in the pneumonectomy space escaped between the diaphragmatic prosthesis and the chest wall to present dramatically as a tension pneumoperitoneum.

Late results Tables VI and VII present the relevant

data for epithelial cases and cases of mixed epithelial and mesenchymal type respectively. There was no statistically significant difference in the ages of these two histological groups. Only one case of pure mesenchymal type was encountered in the surgical series, and the patient unfortunately died in the immediate postoperative period.

Table VIII relates survival to tumour stage and histological type. Statistical analysis of the results in patients who survived operation shows that:

1. Comparing all epithelial cases and all cases of mixed epithelial and mesenchymal type, a significantly higher survival rate ($P < 0.01$) in the epithelial group can be demonstrated only at six months after operation.
2. Comparing all patients with stage I tumours, significantly more of the epithelial group ($P < 0.05$) survived one year or more.
3. Comparing patients of epithelial type, significantly more patients with type A tumours ($P < 0.05$) survived more than two years.

NON-SURGICAL CASES Table IX shows the survival time from the onset of symptoms until death in each histological group. No cases of mixed type or mesenchymal type survived longer than two years, whereas three patients with epithelial type tumours (42.9%) lived three years or longer. Some patients with epithelial tumours obviously have a better prognosis, but taking the group as a whole, there is no statistically significant difference in survival between the patients with epithelial tumours and those with mixed or mesenchymal tumours.

Table X shows the pathological staging of the tumour at necropsy in each histological group. Small numbers make statistical analysis unhelpful but it is interesting to note that 100% of mesenchymal

TABLE VI
DETAILED ANALYSIS OF 11 CASES OF EPITHELIAL TYPE

Case	Age at Operation	Sub-type	Tumour Stage	Lymph Node Involvement	Diaphragm Penetration	Chest Wall Involvement	Post-operative Survival (months)	Total Survival (months) 1st symptom to death	Subsequent Radiotherapy	
									Time Interval (months)	Reason
1	63	B	I	0	0	0	0	4		
2	60	A	I	0	0	0	0	36		
3	62	AB	II	+	0	0	6	8	12	Recurrence in scar
4	48	B	III	0	+	0	7	12		
5	60	B	III	0	+	0	11	23		
6	35	B	I	0	0	0	15	5		
7	57	B	I	0	0	0	16	19		
8	56	B	II	+	0	0	17	23		
9	60	B	II	0	0	+	21	24		
10	49	A	I	0	0	0	41 ¹	65 ¹		
11	57	A	I	0	0	0	75 ¹	123 ¹		

¹Patients still alive.

TABLE VII
DETAILED ANALYSIS OF 17 CASES OF MIXED EPITHELIAL AND MESENCHYMAL TYPE

Case	Age at Operation	Tumour Stage	Lymph Node Involvement	Diaphragm Penetration	Chest Wall Involvement	Post-operative Survival (months)	Total Survival (months) (1st symptom to death)	Subsequent Radiotherapy	
								Time Interval after Operation (months)	Reason
12	61	I	0	0	0	0	11		
13	63	II	+	0	0	0	12		
14	49	I	0	0	0	0	?		
15	59	I	0	0	0	0	9		
16	45	II	+	0	0	0	8		
17	52	II	+	0	0	0	2		
18	55	I	0	0	0	3	5		
19	47	II	+	0	0	3	8		
20	53	I	0	0	0	3	9		
21	50	I	0	0	0	3	9		
22	44	I	0	0	0	4	14	3	Supra-clavicular lymph node metastases
23	47	I	0	0	0	4	6		
24	60	I	0	0	0	4	16	3	Tumour recurrence in wound
25	44	II	+	0	0	8	11		
26	54	I	0	0	0	9	13		
27	38	I	0	0	0	22	30		
28	43	I	0	0	0	24	48	16	Tumour recurrence in chest wall

TABLE VIII

ANALYSIS OF POSTOPERATIVE SURVIVAL RELATED TO HISTOLOGICAL TYPE AND TUMOUR STAGE (HOSPITAL DEATHS EXCLUDED)

	Tumour Stage					
	I		II		III	
Epithelial						
Type A	41 ¹	75 ¹				
Type AB			6			
Type B	15	16	17	21	7	11
Mixed epithelial and mesenchymal	3	3	3	4	4	
	4	9	22	24		

¹Still alive and well.

The figures in the table represent the survival in months for each patient.

tumours had already reached stage IV at the time of death, whereas two of the epithelial tumours (28.6%) were still in stage I in spite of long histories. In both of these patients, death was accelerated by right heart failure secondary to bulk of tumour in the lung and massive pleural effusion.

COMPARISON OF SURGICAL AND NON-SURGICAL CASES
Analysing data from Tables VI, VII, and IX and comparing survival times from first symptom to death in surgical and non-surgical cases, it is not surprising to find that there is no statistically significant difference in the survival of the two groups,

TABLE IX

DETAILED ANALYSIS OF THE NON-SURGICAL NECROPSY SERIES

Case	Histology	Age at Death	Tumour Stage at Death	Total Survival (months) (1st symptom to death)
30	E B	62	IV	10
31	E AB	65	IV	10
32	E B	48	II	11
33	E B	60	III	12
34	E AB	76	I	36
35	E B	75	IV	96
36	E B	67	I	144
37	EM	66	IV	5
38	EM	62	IV	8
39	EM	58	IV	12
40	EM	52	IV	13
41	EM	60	III	18
42	EM	56	II	20
43	EM	62	IV	24
44	M	60	IV	5
45	M	55	IV	8
46	M	61	IV	24

either overall or when analysed for each of the histological types. Operative deaths were excluded from the analysis.

Insufficient information is available from the hospital records of the medically treated cases to make any comparison of morbidity in the two groups.

TABLE X

TUMOUR STAGE AT NECROPSY (NON-SURGICAL CASES)
RELATED TO HISTOLOGICAL TYPE

Histological Type	Tumour Stage			
	I	II	III	IV
Epithelial	28.6%	14.3%	14.3%	42.9%
Mixed epithelial and mesenchymal		14.3%	14.3%	71.4%
Mesenchymal				100%

DISCUSSION

Since diffuse malignant mesothelioma of the pleura was first recognized as a clinical entity there has been controversy about the best form of treatment, and the present multiplicity of treatment regimens testifies to the lack of success of most of them.

The forms of treatment currently practised can be classified as palliative or radical. Most forms of palliative treatment seek to relieve dyspnoea by the prevention of recurrent pleural effusion. Methods advocated for producing pleural symphysis include thoracotomy and poudrage (Prorok and Nealon, 1968), pleuroscopy and poudrage (Scarbonchi and Razzouk, 1967), and simple pleurectomy (Merlier, le Brigand, and Wapler, 1968; Lanitis and Waridel, 1973), the latter having the additional advantage of pain relief. However, the most satisfactory means of achieving pleural symphysis appears to be tube drainage with maintained suction and the introduction of cytotoxic agents (Leininger, Barker, and Langston, 1969; Anderson, Philpott, and Ferguson, 1974), the latter causing adhesion largely by their irritant action on the pleural surfaces. Pain due to chest wall involvement is most effectively relieved by palliative radiotherapy (Schlienger *et al.*, 1969).

The term radical treatment implies the complete elimination of tumour in the hope of achieving a cure. High dose radiotherapy is often referred to as radical or 'aggressive' treatment but, although tumour shrinkage has been reported in some cases (Eschwege and Schlienger, 1973), complete elimination of tumour has never been achieved, and the high doses required have a very detrimental effect on lung function which progresses for 6–12 months. High dose radiotherapy should probably be regarded only as a method of obtaining slightly longer-term palliation.

The only treatment for this disease which can be termed truly radical, therefore, is surgery. Eiselsberg (1922) was the first to recommend radical surgery for diffuse malignant mesothelioma of the pleura but, owing to the limitations of thoracic surgery at that time, he did not remove the whole lung. Subsequent authors (Harris, Hyman, and Nevins, 1959; Saltzer, 1959; Jagdschian, 1962 and 1970) advocated pleuro-

pneumectomy as the treatment of choice for this condition, and the first pleuropneumectomy for diffuse malignant mesothelioma in this clinic and also probably the first in this country was performed by Mr. G. A. Mason in February 1949 (because of incomplete records the patient was not included in the present series).

The fact that two patients in the series are still alive and well and free from recurrence 3½ and 6 years respectively after pleuropneumectomy shows that the operation can be successful. Nevertheless, the generally poor results obtained in this series and in others (Ehrenhaft, Sensenig, and Lawrence, 1960; Porter and Cheek, 1968; Hertzog and Toty, 1968; Merlier *et al.*, 1968; Seliverstov, 1970; Bartoszewicz, 1971; Lanitis and Waridel, 1973) necessitate a re-appraisal of the place of pleuropneumectomy. Some authors (Hertzog and Toty, 1968; Merlier *et al.*, 1968; Schlienger *et al.*, 1969; Herrmann and Herrmann, 1972) have condemned the operation on the grounds of its high immediate mortality, the difficulty in achieving tumour clearance, the risk of seeding tumour in the chest wall, and the poor long-term survival figures. The unsubstantiated view that surgical treatment may result in distant metastases (Elmes, 1973b) has been refuted by Whitwell (1973). Previous authors have not related their results to histological type or to tumour stage, and, with the exception of Elmes (1973a and 1973b), who studied cases from several centres in Great Britain and cases from the literature, all authors draw conclusions from personal experience of small numbers of cases, the largest series being that of Hertzog and Toty (1968), who reported six cases.

With personal experience of a much larger number of cases, certain points emerge which enable an attempt to be made to answer the criticisms against radical surgery:

1. High mortality alone should not condemn an operation but should stimulate thought into means of reducing the mortality. In our series, seven out of nine deaths were considered preventable by better case selection, improved surgical technique or better postoperative management.
2. The margin of tumour clearance in pleuropneumectomy is necessarily small but in many cases of diffuse malignant mesothelioma this is adequate as the disease remains confined to the pleura for a long time, showing little inclination to invade the adjacent skeletal muscle of the chest wall (Jagdschian, 1970). Where chest wall invasion has taken place multifocally the patient is not suitable for pleuropneumectomy.

3. Studying survival in relation to histological type and pathological staging and planning management accordingly is now practised for most tumours, and mesothelioma should be no exception.

When this procedure is applied to mesothelioma it is possible to identify a group of patients whose prognosis justifies the application of radical surgery.

SIGNIFICANCE OF HISTOLOGICAL TYPING In necropsy studies, Whitwell and Rawcliffe (1971) found distant metastases from epithelial tumours much less frequent than from tumours containing mesenchymal elements. These findings correlate well with our own necropsy series (Tables IX and X). Although further work is necessary on the subject, it appears from our results that the mesenchymal element of mesothelioma, whether occurring in pure form or mixed with the epithelial element, renders the tumour more malignant. The epithelial element when it occurs in pure form appears to carry a better prognosis, particularly when it is composed entirely of type A. Only three cases of type A epithelial tumours were seen (Table VI) in the surgical series; all three had long histories before operation and the two who survived operation are both alive and well with no recurrence. It is interesting that no case of pure epithelial type A was encountered in the non-surgical necropsy series and that the two long-term survivors (cases 35 and 36) were both of type B.

There seems little doubt that mesenchymal tumours, pure or mixed, have a poor prognosis and do not justify radical surgery. Examination of a larger series of epithelial cases is required to clarify the association of type A tumours with prognosis, and it is our opinion, therefore, that all stage I epithelial tumours should be given the opportunity of radical surgery.

CLINICAL STAGING OF MESOTHELIOMA Mediastinal lymph node involvement can be assessed by mediastinoscopy and macroscopical diaphragmatic penetration by radiology of the undersurface of the diaphragm using artificial pneumoperitoneum. Although there are no reports in the literature of the latter technique being used in diffuse malignant mesothelioma, its value in outlining other diaphragmatic pathology has been reported (Trimble and Leftwich, 1955; Stevens and McCort, 1964; Meyers, 1973). Extensive or multifocal chest wall invasion should contraindicate radical surgery. However, we are in agreement with Jagdschian (1970) in believing that the tumour is rarely locally inoperable in this way.

MANAGEMENT OF THE INDIVIDUAL CASE The following plan of management (Fig. 5) is suggested for patients presenting with diffuse malignant mesothelioma of the pleura:

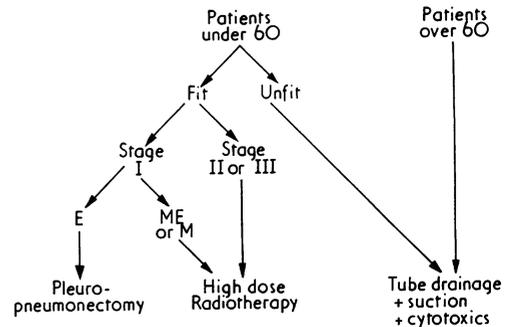


FIG. 5. Schematic representation of the management of diffuse malignant mesothelioma of the pleura: E = epithelial type; ME = mixed epithelial and mesenchymal type; M = mesenchymal type.

1. Exclude patients over the age of 60, unless exceptionally fit, from consideration for radical surgery, because of the high mortality rate in this age group.
2. In patients under 60, carry out detailed assessment of respiratory and cardiac status. The patient's account of his exercise tolerance before the onset of symptoms is important. Evidence of ischaemic heart disease, moderate or severe chronic bronchitis, emphysema, excessive obesity or any disease likely to affect the function of the remaining lung should contraindicate surgery and high dose radiotherapy. These patients should receive palliative treatment.
3. In those patients considered fit for major surgery, proceed to:
 - (a) mediastinoscopy. Obtain mediastinal lymph nodes for biopsy. Involved lymph nodes should contraindicate pleuropneumectomy.
 - (b) artificial pneumoperitoneum and radiology of the undersurface of the diaphragm. This should have a smooth concave surface and anything to suggest penetration by tumour should contraindicate surgery.
4. If the investigations above suggest that the tumour has not progressed beyond stage I, proceed to open pleural biopsy and frozen section histology. An accurate histological diagnosis, identifying the type of mesothelioma, requires a large sample of tumour (needle biopsy is therefore unsuitable), as it is possible

for some parts of the tumour to appear entirely epithelial and others mesenchymal.

5. Proceed to pleuropneumectomy only if frozen section histology shows the tumour to be of pure epithelial type.
6. In all fit patients with mixed and mesenchymal histological type and in stage II cases of epithelial type, the use of high dose radiotherapy may be worth while to achieve somewhat longer-term palliation.
7. In those patients unfit for either surgery or high-dose radiotherapy, the best form of palliation appears to be a combination of tube drainage with maintained suction and intrapleural cytotoxic drugs.

PREVENTION OF HOSPITAL MORTALITY AND MORBIDITY
If pleuropneumectomy is to be recommended for selected cases of diffuse malignant mesothelioma, means of reducing the operation's present high mortality and morbidity must be sought. Careful cardiorespiratory assessment and exclusion of high-risk patients as detailed above should substantially reduce the incidence of respiratory failure post-operatively. Further reduction in the complication rate can be achieved only by attention to operative technique and postoperative management.

During the operation care should be taken to secure haemostasis as the operation proceeds, rather than leaving haemostasis until the specimen is removed. In this way very large blood losses and the risks of rapid blood transfusion can be avoided. Particular attention should be paid to haemostasis during the separation of the diaphragm from its peripheral attachments or large amounts of blood may drain into the peritoneal cavity and remain unaccounted for. If haemostasis is incomplete in this situation, bleeding into the peritoneal cavity may continue postoperatively to produce unexplained hypovolaemia.

Sound suturing of the diaphragmatic prosthesis to the chest wall is essential and is more easily accomplished if the prosthesis is sited higher than the original diaphragm.

Postoperative management should be undertaken in a cardiothoracic intensive care unit. Every effort should be made to achieve optimum haemodynamic status, ventilation, and acid-base balance within the first few hours after surgery, if necessary instituting artificial ventilation until the day after operation.

CONCLUSIONS

Pleuropneumectomy is a formidable operation and our results show that it cannot be justified as the treatment of choice for all cases of diffuse malignant mesothelioma of the pleura. However, if the hospital

morbidity and mortality can be reduced, it seems justified to recommend the operation for stage I cases of pure epithelial type.

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REFERENCES

- Anderson, C. B., Philpott, G. W., and Ferguson, T. B. (1974). Treatment of malignant pleural effusions. *Cancer*, **33**, 916.
- Ashcroft, T. (1973). Epidemiological and quantitative relationships between mesothelioma and asbestos on Tyneside. *Journal of Clinical Pathology*, **26**, 832.
- Bartoszewicz, T. (1971). Złoslíwe miedzybloniaki oplucnej (malignant pleural mesotheliomas). *Polski Przegląd Chirurgiczny*, **42**, 1733.
- Ehrenhaft, J. L., Sensenig, D. M., and Lawrence, M. S. (1960). Mesotheliomas of the pleura. *Journal of Thoracic and Cardiovascular Surgery*, **40**, 393.
- Eiselsberg, A. v. (1922). Im Protokoll der Gesellschaft der Ärzte in Wien. *Wiener klinische Wochenschrift*, **509**.
- Elmes, P. C. (1973a). The natural history of diffuse mesothelioma. In *Biological Effects of Asbestos*, pp. 267–272. The International Agency for Research on Cancer, Lyon, France.
- (1973b). Therapeutic openings in the treatment of mesothelioma. In *Biological Effects of Asbestos*, pp. 277–280. The International Agency for Research on Cancer, Lyon, France.
- Eschwege, F. and Schlienger, M. (1973). La radiotherapie des mesotheliomes pleuraux malins. *Journal de Radiologie, d'Electrologie et de Médecine Nucleaire*, **54**, 255.
- Harris, M. S., Hyman, M. M., and Nevins, D. B. (1959). A resectable form of multiple mesothelioma. *Diseases of the Chest*, **35**, 127.
- Herrmann, von K. and Herrmann, R. M. (1972). Probleme der Diagnostik und Behandlung von Pleuramesotheliomen. *Archiv für Geschwulstforschung*, **40**, 355.
- Hertzog, P. and Toty, L. (1968). Prognostic du traitement chirurgical des tumeurs malignes primitives de la plevre. *Poumon et le Coeur*, **24**, 529.
- Hourihane, D. O'B. (1964). The pathology of mesotheliomata and an analysis of their association with asbestos exposure. *Thorax*, **19**, 268.
- Jagdschian, V. (1962). Tumoren der Pleura. Pathologie, Klinik und Therapie an Hand von 26 eigenen Beobachtungen. *Ergebnisse der Chirurgie und Orthopädie*, **44**, 201.
- (1970). Das Pleuramesotheliom—Häufigkeit und Behandlung. *Thoraxchirurgie*, **18**, 428.
- Lanitis, G. and Waridel, D. (1973). Les tumeurs primitives de la plevre. *Revue Médicale de la Suisse Romande*, **93**, 115.

- Leininger, B. J., Barker, W. L., and Langston, H. T. (1969). A simplified method for management of malignant pleural effusion. *Journal of Thoracic and Cardiovascular Surgery*, **58**, 758.
- McCaughy, W. T. E. (1958). Primary tumours of the pleura. *Journal of Pathology and Bacteriology*, **76**, 517.
- (1965). Criteria for diagnosis of diffuse mesothelial tumours. *Annals of the New York Academy of Sciences*, **132**, 603.
- Merlier, M., Le Brigand, H., and Wapler, C. (1968). Chirurgie des tumeurs pleurales primitives. *Poumon et le Coeur*, **24**, 521.
- Meyers, M. A. (1973). Peritoneography. Normal and pathologic anatomy. *American Journal of Roentgenology*, **117**, 353.
- Porter, J. M. and Cheek, J. M. (1968). Pleural mesothelioma. *Journal of Thoracic and Cardiovascular Surgery*, **55**, 882.
- Prorok, J. and Nealon, T. F. (1968). Pleural symphysis by talc poudrage in the treatment of malignant pleural effusion. *Bulletin de la Société Internationale de Chirurgie*, **27**, 630.
- Salzer, G. (1959). Die diffusen Pleuratumoren als chirurgisches Problem. *Thoraxchirurgie*, **7**, 377.
- Scarbonchi, J. and Razzouk, H. (1967). Traitement palliatif des épanchements pleuraux neoplastiques. *Marseille-Médical*, **104**, 939.
- Schlienger, M., Eschwege, F., Blache, R., and Depierre, R. (1969). Mesotheliomes pleuraux malins. Etude de 39 cas dont 25 autopsies. *Bulletin du Cancer*, **56**, 265.
- Seliverstov, V. E. (1970). Radikalnaia operatsiia pervichnoi diffuznoi mezoteliome plevry. *Grudnaya Khirurgiya*, **12**, 104.
- Stevens, G. M. and McCort, J. J. (1964). Abdominal pneumoperitoneography. *Radiology*, **83**, 480.
- Trimble, H. G. and Leftwich, W. B. (1955). The diagnostic use of artificial pneumoperitoneum. *Diseases of the Chest*, **28**, 282.
- Wagner, J. C. (1971). Asbestos and cancer. In *Deeley, S. Modern Radiotherapy: Carcinoma of the Bronchus*, p. 41.
- Whitwell, F. (1973). Discussion following the papers of P. C. Elmes. In *Biological Effects of Asbestos*, p. 281. The International Agency for Research on Cancer, Lyon, France.
- Whitwell, F. and Rawcliffe, R. M. (1971). Diffuse malignant pleural mesothelioma and asbestos exposure. *Thorax*, **26**, 6.

Requests for reprints to: Dr. T. Ashcroft, Consultant Pathologist, Leighton Hospital, Crewe, Cheshire.