somewhat with our mode of living. Perhaps it may prove to be correlated with the great increase in tobacco consumption.

Integration

It does not seem possible to integrate the many aetiological considerations into one neat explanation, and it is probable that peptic ulcer is the end-product of a variety of mechanisms. Furthermore, the independent behaviour of gastric and duodenal ulcer in relation to social class, occupational incidence, and hereditary and epidemiological factors does suggest that different mechanisms may be operating, although there may well be many factors common to both sites.

How can all the differences in incidence be related to the causation of peptic ulcer? First, there must be environmental factors which account for the changing incidence in this century and the varying incidence in different parts of the world. Secondly, there must be hereditary constitutional factors which help to determine the incidence and site of ulcers. These must include the secretory cell mass of the stomach and the blood groups. Some members of the community may have a special liability to duodenal ulcer by virtue of their specially generous endowment with parietal cells or because of their blood group.

From the pathological viewpoint there is less difficulty in explaining acute than in explaining chronic ulcers. Probably acute gastric lesions—small superficial ulcers—are very common and widely distributed over the stomach and duodenum, and normally heal rapidly. From the frequent presence of mucosal fragments in gastric aspirations such small lesions are known to occur (Hawksley and Cooray, 1948). Such small lesions may be part of the normal life-cycle of the epithelium or could be due to some cytotoxic factor analogous to aphthous ulcers in the mouth. It is also possible that local ischaemia from vascular spasm could cut off adequate supplies of carbon dioxide from actively secreting parietal cells, and this could lead to an intracellular necrotizing concentration of alkalis. Davis (1952) has produced experimental ulcers this way.

The real problem in peptic-ulcer pathology is, why do some ulcers become chronic? This may be due to the presence of anti-healing factors, which could be either humoral or exogenous. The healing process could be modified by adrenal overactivity from mental or physical stress or by administration of cortisone or corticotrophin. This could operate either on cellular repair mechanisms or by modifying the physical character of mucus as suggested by Hirschowitz, Streeten, Pollard, and Boldt (1955). An impaired mucous barrier might allow cytotoxic factors within the stomach more ready access to the damaged mucosa. It is quite conceivable that anti-healing factors could be present in food and might determine the striking differences in geographical distribution. Tapioca root is the staple diet in Southern India and also in Southern Nigeria, where duodenal ulcers are so prevalent. Could the appreciable amounts of hydrocyanic acid in the root act as an anti-healing factor? Another possible anti-healing influence might arise from vascular constriction. In chronic ulcers the blood supply at the base of the ulcer may become so diminished by vascular occlusion that healing is no longer possible (Key, 1950). An earlier phase might be functional vasoconstriction from tobacco smoking.

Daintree Johnson (1955) believes that stasis in the stomach could be correlated with the development of gastric ulcer. Stasis in a jejunal loop or in the duodenum might also play a part as an anti-healing factor. Possibly the volume of secretion, and especially pooling, of gastric juice may have a greater anti-healing effect than the mere level of acidity. Stasis plus hypersecretion may be a particularly potent combination. In this connexion it is interesting to recall the observation of Zollinger and Ellison (1955), who found an association between the presence of non-insulin-secreting adenoma of the pancreas and sustained hypersecretion leading to stomal ulcer. Another mechanical factor might be the force of the jet of gastric juice passing through the pylorus and impinging on the duodenal cap, and this in turn could be correlated with nervous tension reflected on gastric motor activity.

Gastric and duodenal ulcers can occur in lower animals but only rarely in the natural state. Natural selection would tend to eliminate animals prone to develop ulceration from unusual environmental factors. In man new personal habits, new foods, new drinks, new methods of cooking and food preparation, and changing feeding habits have come under the guise of civilization. The forces of natural selection have become blunted by medical science, and a disequilibrium now exists between man and his environment, and one of its manifestations is peptic ulcer.

[The second lecture, with a list of references, will appear in our next issue.]

REVIEW OF 464 CASES OF CARCINOMA OF LUNG TREATED BY RESECTION

BY

JOHN HAMILTON GIFFORD, M.B., C.P.H.

AND

J. K. B. WADDINGTON, M.B., F.R.C.S.Ed.

From the Thoracic Surgical Unit, Broadgreen Hospital, Liverpool

In his Lister lecture of 1947 Graham reported the first substantial series of cases of carcinoma of the lung treated by pneumonectomy. Since then numerous papers have recorded the results of individual surgeons or groups of surgeons in different parts of the world.

In Great Britain, Sellors, Cruickshank, and Billimoria (1947) reported a series, followed by Brock (1948), Mason (1949), Taylor and Waterhouse (1950), Price Thomas (1952), Sellors (1955), Bignall and Moon (1955), and Belcher (1956).

At the present moment surgical treatment, where possible, is generally accepted as the most satisfactory treatment for bronchial carcinoma. This involves removal of between a quarter and a half of the respiratory mechanism, and the ability of the patient to withstand the operation depends on the function of the remaining lung tissue and his cardiovascular system. In a heavy industrial and climatically severe region such as Liverpool, inflammatory and degenerative changes in the two systems, especially in the 40 to 60 age group, are likely to be more pronounced than in the districts where sedentary occupations and light industries predominate. That such changes will affect the results of surgery is only too obvious, and it is against this background that we have investigated the results of surgery in the Liverpool Region. As a regional centre, the thoracic unit undertakes most of the surgical treatment of cases in the area apart from the few that gravitate elsewhere. We have based the figures on the known incidence of the disease in this area as revealed by the Cancer Control Organization.

The basis for selection, and the operability, operative mortality, and survival rates vary from author to author, so that a true comparison of results is not readily available. To provide some measure of comparison we have

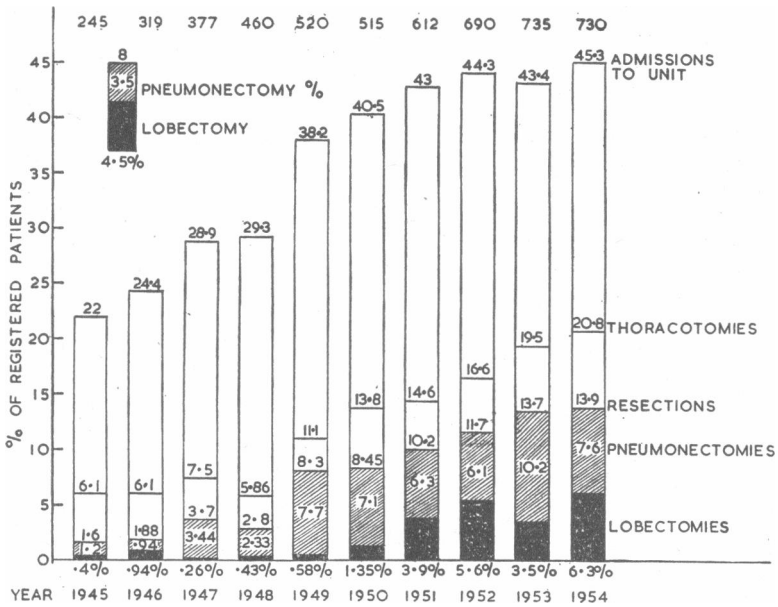

FIG. 1.—Carcinoma patients admitted to unit, thoracotomies performed, and tumours excised, expressed as percentages of patients registered each year by the Cancer Control Organization. (Proportions of patients treated by lobectomy or pneumonectomy represented by black and shaded columns respectively.)

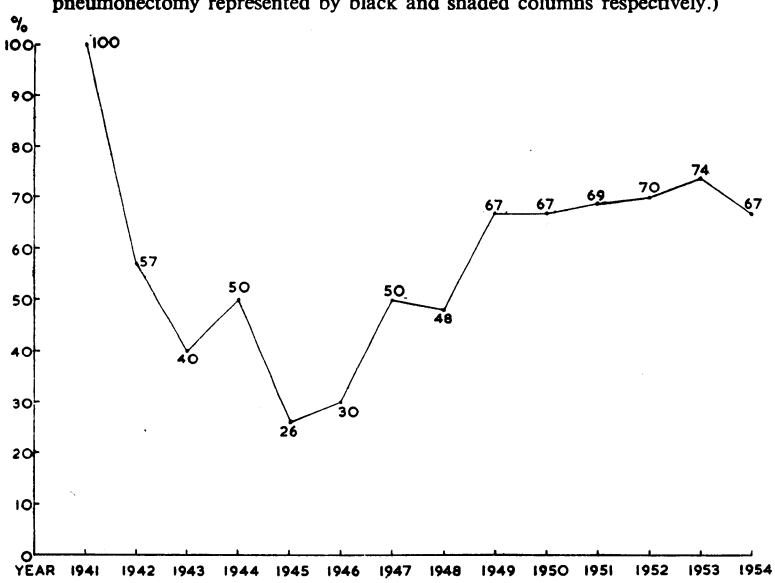

FIG. 2.—Proportion of thoracotomies in which resection was possible for each year from 1941 to 1954.

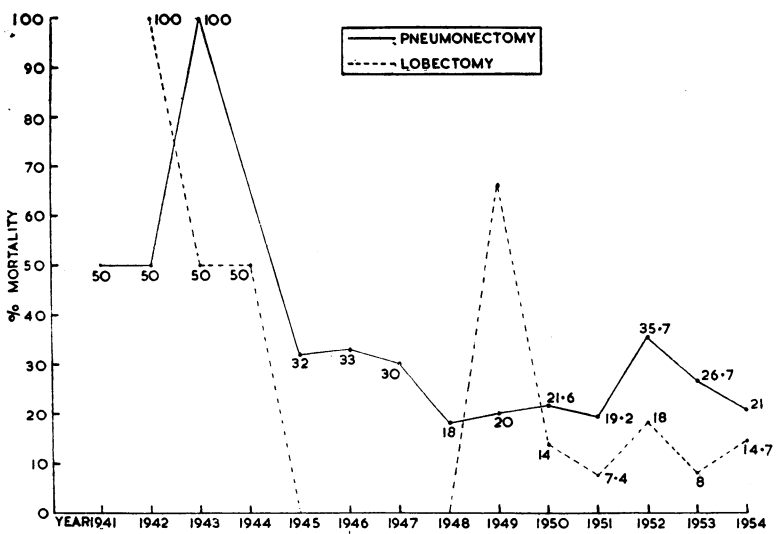

FIG. 3.—Annual operative mortality from pneumonectomy and lobectomy.

adopted the same criteria as Bignall and Moon (1955) and Belcher (1956) for the operative mortality, survival rate, and histological groups.

In December, 1955, we reviewed all the cases of bronchial carcinoma admitted to the Liverpool Thoracic Surgical Unit between 1941 and 1954. Figures are available for the cases registered each year by the Liverpool Cancer Control Organization from 1945 onwards, and these are quoted at the top of Fig. 1. The Organization covers substantially thesame region as the Liverpool Thoracic Unit and gives a reliable figure for the known incidence of the disease for the area.

A total of 2,156 patients suffering from bronchial carcinoma were admitted to the unit, of which 7% were women. Of these, 714 were explored (33%) and from 464 (21%) the growths were removed.

Fig. 1 shows the annual percentages of registered patients who were admitted to the unit, were subjected to thoracotomy, and from whom the growth was excised. The relative proportions of lobectomies and pneumonectomies by which the tumour was removed are also shown (calculated to nearest 0.1%).

The proportion of notified cases admitted to the unit increased steadily from 22% in 1945 to 45% in 1954, whilst in the same period the numbers explored rose from 6.1% to 20.8%. Thus the thoracotomy rate increased from an average of 6.4% between 1945 and 1949 to 15% in the period 1950–2 and 20% in 1953–4. This is the natural result of earlier diagnosis, M.M.R. services, and improved clinical facilities, aided more recently by external diagnostic endoscopic clinics at which the obviously inoperable cases were eliminated.

Similarly, the numbers of patients from whom the growths were excised increased from 1.6% in 1945 to 13.9% in later years; there has therefore been approximately a ninefold improvement in the chance of a patient having his tumour removed.

Between 1941 and 1948 the average ratio of operable to inoperable growth was 3 : 4, but from 1949 onwards this averaged 7 : 3. Whilst the number of resections has increased from year to year, the relative proportions of pneumonectomies and lobectomies altered considerably, and, whereas pneumonectomy was the more usual operation prior to 1951, that year marked a change of policy, and in subsequent years the numbers of lobectomies increased considerably.

Not only does pneumonectomy carry a higher operative mortality than lobectomy, but the loss of a whole lung deprives the patient of a larger volume of functioning lung tissue, and this may lead to respiratory insufficiency

amounting in some cases to respiratory crippledom. With this in mind, it has been the policy to perform lobectomy in all possible cases, provided the basic criteria for effective removal of the tumours were fulfilled.

The proportion of thoracotomies in which removal of the tumour has been possible is shown in Fig. 2. This had increased since 1945, and though in later years it showed slight variations, during each of the last six years approximately 70% of the growths were removable. No doubt this figure could be improved by rejecting doubtful or borderline cases, but by so doing many patients would be deprived of the benefits of surgery.

Material.—The percentage of patients in quinquennial age groups was: under 45 years, 14.8% ; 45–49, 18% ; 50–54, 24.5% ; 55–59, 23.7% ; 60 and over, 19%. Of the 464 patients in whom resection of the tumour was possible, 448 were followed to death or for a minimum of one year.

Operative Mortality

Operative mortality is defined as the number of patients undergoing operation who died of any cause within two months, expressed as a percentage of the whole.

Of the 464 patients undergoing operation, 101 (21.7%) died within two months. Prior to 1948, 31% died, but as the number of operations and experience increased so the mortality fell to 21.5% for the years 1949 to 1954. The respective mortalities for pneumonectomy and lobectomy were 25.9% and 14.7%, showing that the former carried a higher operative risk.

Only 33 women underwent operation, and of these 12% died—a proportion much less than that for men.

Fig. 3 shows the annual variation in operative mortality for pneumonectomies and lobectomies. With the exception of peaks in 1943 and 1952, the mortality for the former declined from 50% in 1942 to 21% in 1954. Lobectomies showed more variation from year to year, but after 1950, when they were performed more often, the mortality became more uniform, with an average of 12.4%.

Comparison with Other Series.—Table I shows the operative mortality recorded by various authors. The mortality in the Liverpool series is strictly comparable only to that of Bignall and Moon, to whose criteria for operative mortality we adhered in calculating the operative deaths. As might be expected, the operative mortality for pneumonectomy has decreased from 53% in Graham's series (Table I) to 11% in Brock and Whytehead's series of "Radical Pneumonectomies," and, although Bignall and Moon reported no deaths from lobectomy, the average mortality for this operation ranges from 4.5 to 9% in the hands of different surgeons.

To determine, if possible, how operative risk could be reduced, we investigated the cause of death in all cases (Table II). The deaths are grouped into "early," occurring within 48 hours of operation, and "late," occurring after 48 hours but within two months, and we found that 42 patients (41.6% of deaths) died within 48 hours.

Accidental or technical difficulties accounted for 12.87% of deaths, coronary thrombosis or congestive failure caused 24.75%, pulmonary embolism and cerebral thrombosis accounted for 2.97% and 2.97% respectively, and a further group due to pulmonary oedema, insufficiency, or infection totalled 31.68%. No fewer than 62.37%, therefore, were due to pulmonary deficiency or vascular lesions of brain, heart, or lungs.

Putting this group into a category of "cardio-pulmonary failure" (C.P.F.), we have in Table III related the proportion of C.P.F. deaths to the total early and late deaths occurring after right and left pneumonectomies and lobectomies.

Whilst the numbers of right and left pneumonectomies were similar, there was a marked difference in the mortality for the two sides, the right being nearly twice that of the left (33% against 17.3%). The numbers of lobectomies differed somewhat, and the contrast between the two sides was not so pronounced, but, even so, 16.3% of patients who had right lobectomies died, compared with 11.7% of left. When only the C.P.F. deaths are considered the contrast is even greater.

Bignall and Moon also found a higher mortality for right-sided operations (right 12%, left 8%), but thought chance played a part in the difference.

In our series the contrast was more marked, and we believe that the difference is too great for chance to be the only factor.

Table IV shows the proportion of operations and deaths due to pneumonectomy and lobectomy as they are distributed in quinquennial age groups. Deaths after lobectomy increased with age, but deaths after pneumonectomy showed

TABLE I.—*Operative Mortality of Other Reported Series*

Author	Resection	Mortality Rate
Graham (1947)	Pneumonectomy	53%
Rienhoff (1947) ..	,,	22·3%
Sellors *et al.* (1947) ..	,,	15%
Brock (1948)	,,	18%
Mason (1949)	,,	12·5% (within 1 month)
Taylor and Waterhouse (1950)	,,	24·3% (within 3 months)
Sellors (1955)	Pneumonectomy (364)	24% (1940–8)
	Lobectomy (82)	9% (1948–50)
Brock and Whytehead (1955)	Radical pneumonectomy	11%
Bignall and Moon (1955)	Pneumonectomy	13% (1950–1)
	Lobectomy	0% (1950–1)
Belcher (1956)	Lobectomy	4·5%
Liverpool (1956) ..	Pneumonectomy	25·9% } Total series
	Lobectomy	14·7% }
	Pneumonectomy	19·2% } 1951
	Lobectomy	7·4% }

TABLE II.—*Cause of Death in "Early" and "Late" Phases*

Cause	Early			Late			Total
	No.	Age Group	Av. Age	No.	Age Group	Av. Age	
D.O.T.	4	45–53	50				
Haemorrhage ..	4	44–50	47	2	63–64	63	12·87%
Shock	3	48–63	57				
Coronary thrombosis or congestive failure	9	47–66	51	16	51–68	60	24·75%
Pulmonary embolism	2	40–46	43	1		53	2·97%
Cerebral thrombosis	2	50–56	55	1		50	2·97%
Pulmonary oedema or insufficiency infection	10	45–59	55	8	45–60	53	17·82%
	5	46–61	56	9	45–63	54	13·86%
Metastasis	1		45	7	45–59	48·5	7·92%
Saddle embolus (tumour)	1		57				0·99%
Uraemia (prostatic) ..				4	54–71	62	3·96%
B.P. fistula				8	30–61	52·6	7·92%
Perf. D. ulcer ..				2	48–61	52	1·98%
Pericarditis	1		62	1		51	1·98%
Total	42			59			101

TABLE III.—*Operative Mortality*

Operation	Early		Late		Totals	
	C.P.F.	All	C.P.F.	All	C.P.F.	All
Pneumonectomies:						
Right (151) ..	12·8%	16·5%	11·2%	17·8%	24%	33%
Left (161) ..	4·3%	6·2%	6·2%	11·1%	10·5%	17·3%
Lobectomies:						
Right (85) ..	3·5%	5·8%	8·2%	10·5%	11·7%	16·3%
Left (51) ..	0%	2%	2%	9·8%	2%	11·8%

TABLE IV.—*Effect of Age on Operative Mortality*

Age Group	Whole Series (464)	Pneumonectomies. Deaths (81)	Lobectomies. Deaths (20)
Under 45 ..	15%	8·6%	0%
45–49	18%	17·2%	10%
50–54	24%	28·4%	20%
55–59	24%	16%	30%
60+	19%	29·6%	40%

considerable variation, being most frequent in the 50–54 and 60+ groups. Only 16% fell into the 55–59 group, and it is significant that this particular age group had the highest number of survivors of the operative phase and the best two-year and five-year survival rates.

Survival Rate

The survival rate has been calculated from the formula:

$$\frac{\text{Actual survival}}{\text{Possible survival}} \times 100$$

The fate of 347 patients who survived the arbitrary two months after operation has been reviewed. At the time of review 204 were known to be dead, and, except in those cases where the patient died in hospital and necropsy was possible, the cause of death was obtained from the practitioner who attended during the terminal illness.

The cause was unknown or unspecified in 15 (7.3%), but of the remainder, 152 (74%) died of recurrence or metastasis. Bronchopleural fistula (or sequelae), coronary disease, and pulmonary insufficiency accounted for 8.8%, 3.8%, and 2.4% respectively.

Malignancy was the cause of death of 76% of those who had lobectomy and of 74% of those who had pneumonectomy, 64% and 60% respectively within two years. The proportion of patients dying of malignant disease increased each month to a peak at 18 months, and, whilst four patients died of metastases five years after their pneumonectomy, no patient died of metastases later than three years after lobectomy. As is shown below, the peak at 18 months corresponds with the time at which nodal involvement began to affect survival rates.

The two-year survival rates for pneumonectomies and lobectomies were similar (44% and 45%), but the five-year rate for pneumonectomies (30%) was much more favourable than that for lobectomies (12.5%). Nevertheless, the lobectomy patients have probably survived in greater comfort.

Of the patients alive and well at the time of the survey, 10 had lived for five years, 9 for six, 3 for eight, 2 for nine, and 1 for ten years after pneumonectomy; a total of 25 out of the first 136 patients operated on since 1941 (100 of these survived operation).

Factors Affecting Survival

Table V shows little difference in the two-year and five-year survival rates for patients treated before and after 1948, so that the year of operation seems to have little effect on survival.

Position of Tumour

The tumours were distributed more or less equally between the right and left lungs (170 and 177), and the two-year survival rates were very similar. The five-year rates, however, were much better for right-sided tumours (34% against 22%). The distribution of individual histological types of tumour was even throughout all lobes and both lungs except the left lower lobe, which had 41% undifferentiated types, some 7% more than the average for both lungs. Nodal involvement occurred in 38% of left-sided tumours compared with only 28% of right-sided lesions. This factor, the higher proportion of undifferentiated tumours in the left lower lobe, and cross-lymphatic spread probably accounted for the poorer five-year rate for left-sided tumours.

The survival rates for individual lobes and their histological types were calculated (Table V, Figs. 4 and 5). The left upper lobe was most often involved and the right middle lobe least often. The latter was involved in only 12 cases, and none lived as long as three years after operation.

Of all lobes, the right lower carried the best prognosis, probably by reason of a slightly higher proportion of squamous tumours (Table VI, Fig. 4), a low rate of nodal involvement (25%), the earlier incidence of symptoms, and the fact that, except in basal segmental tumours, it has been the practice to perform a middle and lower lobectomy in nearly all lower lobe tumours.

TABLE V.—*Survival Rates for Patients Living More than Two Months After Operation Related to Period of Operation, Histological Type, Side, Lobe, Age, Sex, and Extent of Operation*

	No.	Survival Rates (%)				
		1 Yr.	2 Yrs.	3 Yrs.	4 Yrs.	5 Yrs.
All patients	347	67	44·6	37	35	28
1941–8	33	70	48	36	36	30
1949–54	314	66	44·1	38	35	25
Squamous	192	71	54	47	43	38
Adenocarcinoma	35	68	31	30	20	—
Undifferentiated	120	57	35	29·3	29·3	19
Right lung	170	62	42	39	35	34
Left ,,	177	72	46	39	36	22
Right upper lobe	63	58	41	37	30	29
Squamous	34	62	55	56	50	37
Adenocarcinoma	12	64	27	22	14	—
Undifferentiated	17	50	27	27	19	28
Right lower lobe	87	69	53	50	46	38
Squamous	50	69	53	50	46	38
Adenocarcinoma	8	66	33	66	50	—
Undifferentiated	29	58	48	44	46	33
Right middle lobe	12	33	10	—	—	—
Left upper lobe	98	82	52	40	40	21
Squamous	55	90	60	56	50	36
Adenocarcinoma	9	77	27	20	25	—
Undifferentiated	34	69	44	28	31	9
Left lower lobe	74	63	38	28	27	22
Squamous	39	69	45	28	29	33
Adenocarcinoma	5	80	33	50	—	—
Undifferentiated	30	53	31	25	28	12
Men	318	68	45	39	37	29
Women	29	67	38	19	23	25
Pneumonectomy	233	64	45	39	37	29
Lobectomy	114	73	44	36	27	12·5
Age under 45	60 (17%)	66	38	38	30	23
45–49	64 (18·4%)	64	42	37	46	42
50–54	83 (23·9%)	72	50	40	32	25
55–59	86 (24·7%)	71	53	45	48	45
60–64	40 (11·5%)	52	33	25	30	—
65 and over	14 (4%)	60	33	33	14	—

TABLE VI.—*Histological Type Related to Period of Operation, Site of Tumour, Sex, Age, Extent of Operation, Nodal Involvement, and Survivors*

	Squamous		Undifferentiated		Adenocarcinoma		Total
	No.	%	No.	%	No.	%	
All patients	192	55	120	34	35	10	347
Right lung	95	56	54	32	21	12	170
Left ,,	97	55	66	37	14	8	177
Right upper lobe	34	55	17	27	11	18	62
,, lower ,,	50	57	29	33	9	10	88
,, middle ,,	5	42	6	50	1	8	12
Left upper lobe	55	56	34	35	9	9	98
,, lower ,,	39	53	30	41	5	7	74
Right main bronchus	6	66	2	33	—	—	8
Left ,, ,,	3	60	2	40	—	—	5
Men	182	56	105	34	31	10	318
Women	10	35	15	52	4	13	29
Pneumonectomy	130	55	86	37	17	7	233
Lobectomy	62	54	34	30	18	16	114
Age under 45	29	47	28	47	3	5	60
45–49	30	48	26	40	8	12	64
50–54	52	63	20	24	11	13	83
55–59	49	56	27	32	10	12	86
60–64	25	61	14	36	1	2·5	40
65 and over	7	50	5	35	2	14	14
Nodal histology:							281
All known cases:							
Nodes free	117	72	55	57	12	55	184
,, involved	46	28	41	43	10	45	97
Two years or more since operation:							
Nodes free	86	70	41	54	9	53	136
,, involved	36	30	35	46	8	47	79
All surviving patients:							
Nodes free	67	57	22	41	6	43	95
,, involved	18	40	8	19	2	20	28

Nodal histology was known in 281 cases and survival time of these was from time of operation to time of survey.

The prognoses for left upper and lower lobe tumours were similar, and were worse than for right-sided tumours, the reasons for this being a higher rate of nodal involvement (30% left upper, 49% left lower), a longer delay in the appearance of symptoms, and cross-lymphatic spread.

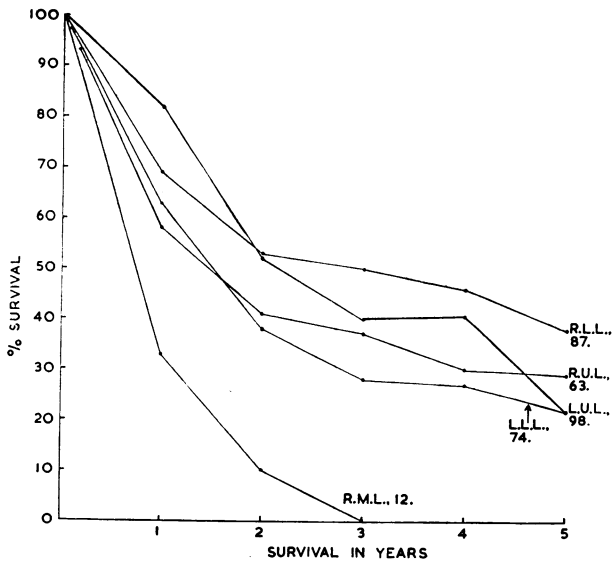

FIG. 4.—Survival rates in upper and lower lobes in both lungs.

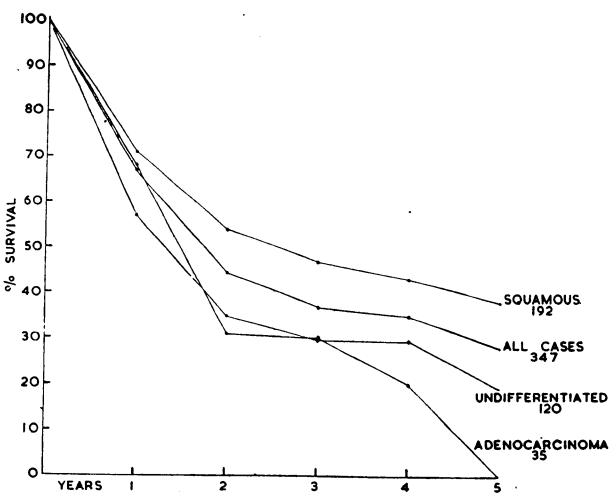

FIG. 5.—Survival rates in the three histological types of tumour.

Age and Sex

The best two- and five-year survival rates were found in the 55–59 quinquennium (53% and 45% respectively), the worst in the over-60 group, 33% of whom survived two years, but none to five years (Table V).

We found that whereas under 50 years of age the distribution of squamous tumours equalled the sum of the undifferentiated and adenocarcinomas—that is, the more malignant types—over this age squamous tumours amounted to 57% of the whole. Nodal involvement by tumour cells occurred in only 29% of patients in the 55–59 group compared with 45% under 45 years and 34% for all other ages. The higher proportion of squamous tumours and the low incidence of nodal involvement probably explains the good survival of the 55–59 group of patients.

In this series 81% of the patients over 60 died of "metastases" compared with 74% for the series as a whole, despite the fact that squamous tumours predominated. It is possible that some of these patients were labelled "metastatic deaths" when in fact death was due to vascular lesions associated with arteriosclerosis.

There were 33 women in the series, four of whom died from the operation. The two- and five-year survival rates were 38% and 25%, compared with 45% and 29% for men (Table V). Adenocarcinomas and undifferentiated carcinomas predominated—65% compared with 44% for men (Table VI)—and though the average age was lower the degree of nodal involvement was much the same. The poorer prognosis would appear to be related to the predominance of the more malignant types of tumour and possible delay in diagnosis, since bronchial carcinoma is less often anticipated in women.

Histological Type of Tumour

All biopsies, tumours, and lymph nodes were examined by the same team of pathologists from 1946 onwards, so that a uniform appraisement of cell types can be expected, and where a "mixed" tumour occurred the predominant cell type dictated the group into which it was placed (F. Whitwell, personal communication).

The histological type of tumour was known in 347 patients who survived the arbitrary two months' operation phase, and the broad classification into squamous, undifferentiated, and adenocarcinomas was adopted.

Table VI shows the distribution of cell types of the tumours in the two lungs, all lobes, main bronchi, type of operation, sex, age groups, nodes, and all survivors.

Squamous tumours occurred in 55% of all cases and behaved consistently in all lobes, with two- and five-year survival rates of 54% and 38% (Tables V and VI). The proportion of squamous tumours was rather lower than in the series recorded by Bignall and Moon, but the survival rate was similar. Nodal involvement occurred in 28% of all squamous tumours.

Undifferentiated tumours occurred in 34% of the patients, compared with 26% in Bignall's series, and, though the overall two-year rate was the same (35%) (Tables V and VI), the five-year rate was considerably less (19% compared with 26%). The prognosis for this type of tumour varied considerably from lobe to lobe, ranging from a two-year rate of 27% in the right upper lobe to 48% in the right lower lobe, with intermediate percentages of 44% and 31% for the left upper and lower lobes. The five-year rate was much better in the right lower and upper lobes (33% and 28%) than in the left (12% and 9%). Nodal involvement occurred in 43% of these tumours.

Adenocarcinomas behaved very differently in this series compared with those recorded by Belcher and by Bignall and Moon. They occurred in 9% of cases (10% of survivors), compared with 13% and 18% respectively. They were commoner in women, more frequently on the right side than the left, and in most cases were associated with hypertrophic pulmonary osteoarthropathy. Nodal involvement occurred in much the same proportion as in undifferentiated types of tumour—namely, 45%. The prognosis compared very unfavourably with the two series mentioned above, 31% surviving two years and 20% for four years; none lived five years (Table V).

Comparing the survival rates of lobectomies in our series, the two-year rate was only 31%, compared with 69% in Belcher's series of lobectomies.

We therefore found that squamous tumours had the best prognosis and adenocarcinomas to be by far the most malignant, both features contrasting strongly with the findings of Belcher and of Bignall and Moon.

Mediastinal and Hilar Nodal Metastases

In this series the involvement of hilar and mediastinal nodes by tumour cells has been investigated from the histological aspect rather than the surgeon's assessment of nodal involvement at operation. With few exceptions, deliberate clearance of mediastinal nodes has been practised since 1947, and most specimens have been examined histologically for evidence of involvement. Full reports were available for 215 specimens removed two years and 53 five years prior

to the time of review. No evidence of metastases was found in 184 cases, and the survival rates for two and five years were 60% and 33% respectively. Metastases occurred in 97 specimens (Table VII), the two- and five-year rates being 26% and 8%.

TABLE VII.—*Patients Surviving Two Months After Operation Related to Year and Type of Operation, Histological Type of Tumour, Duration of Symptoms, and Presence of Nodal Metastases*

	Pre-1951		1951		1952		1953		1954		
	No.	%	No.	%	No.	%	No.	%	No.	%	
All cases	101		54		51		72		69		347
2-yr. survivors ..	47	47	23	43	23	44	31	43	—	—	
Squamous ..	56	55	25	46	25	50	45	62	41	62	192
Undifferentiated and adenocarcinoma	45	45	29	54	26	50	27	38	28	40	155
Pneumonectomy	85	84	30	56	26	51	52	74	40	58	233
Lobectomy ..	16	16	24	44	25	49	20	26	29	42	114
Average age (years)	50		54		51		51		55		
Av. duration of symptoms:											
All cases (months)	6·3		5·0		4·5		3·7		3·3		
Squamous ..	8·0		4·5		5·0		3·2		3·1		
Undifferentiated and adenocarcinoma ..	4·0		5·4		4·0		4·4		3·4		
Known nodal histology	53	52	44	83	46	85	72	100	66	96	281
Nodes free ..	40	75	31	70	27	59	38	53	48	73	184
,, involved ..	13	25	13	30	19	41	34	47	18	27	97
Survivors, nodes free*	13	29	11	38	14	50	22	60	35	73	95
Survivors, nodes involved ..	1	8	2	16	4	21	9	26	12	67	28
Squamous, nodes free	23	77	19	79	16	67	28	64	31	76	117
Squamous, nodes involved ..	7	23	5	21	8	33	16	36	10	24	46
Total squamous ..	30		24		24		44		41		163
Squamous, two-year survivors:											
Nodes free ..	15	65	10	53	12	75	18	64	—	—	55
,, involved	3	43	1	20	3	38	7	44	—	—	14
Total squamous	18	60	11	46	15	63	25	56	—	—	69
Adenocarcinoma and undifferentiated:											
Nodes free ..	17	74	12	60	11	50	10	36	17	68	67
,, involved	6	26	8	40	11	50	18	64	8	32	51
Undifferentiated only:											
Nodes free ..	15	71	11	73	10	53	5	26	14	70	55
,, involved	6	29	6	27	9	47	14	74	6	30	41

* Survivors in this group taken from time of operation to survey in December, 1955. Percentages corrected for histological type, age, sex, duration of symptoms, and extent of operation related to those with nodal involvement.

The two-year rates are identical with those of Bignall, and, though the five-year rates are lower, they show the same ratio of 4:1 in favour of those without metastases. Since his figures were based on the surgeons' assessment of nodal involvement, it would appear that macroscopic appearances compare closely with histological findings.

After correcting for any of the five other major factors which might affect survival—namely, sex, site, duration of symptoms, extent of operation, and histological type—the two-year rate for patients without evidence of metastases was still 60% and slightly lower at five years (29% compared with 33%). The different survival rates of those without compared with those with metastases is therefore very striking (Table VII).

When the one- and two-year survival rates were compared it became apparent that between these periods the effect of nodal involvement became manifest (Table VII). When no metastases were present the rate fell only from 73% to 60%, whereas in those cases with metastases, the rates fell from 67% to 26%. This corresponds to the period in which the highest number of deaths from metastases occurred—that is, 18 months. The advantage of metastasis-free nodes over involved nodes from two years onwards is approximately 2.5:1 up to four years, and at five years the ratio is better at 3.7:1 (all figures corrected as before). Whilst nearly all the recorded metastatic deaths occur early, the results of finding no evidence of tumour deposits at operation are even more marked at five years than earlier.

The effect of nodal involvement on the survival rates of the three main histological types is shown in Tables VI and IX. Squamous tumours showed a survival rate (to the maximum period after operation) of 57% if the nodes were free from metastases. Even in the 28% of squamous tumours where nodes were involved, the survival rate was still as high as 40%.

Adenocarcinomas and undifferentiated tumours without nodal involvement had survival rates of just over 40%—that is, no better than squamous tumours already showing involvement. Forty per cent. showed nodal involvement and the survival rate was 20%.

Table VIII shows the relationship between the site of tumour and the state of the hilar nodes. Left lower lobe tumours had nodal involvement in 49% of cases, probably accounting for the left lung showing metastases in 40% compared with 30% in the right side. The right middle and lower lobes had 78% and 75% free from metastases, and the left and right upper lobes occupied intermediate positions. The diminished survival rate for left lower lobes is thus accounted for without taking into consideration the assumption that lymph paths cross over to the right side (Rouvière, 1932).

TABLE VIII.—*Condition of Lymph Nodes Related to Individual Lobes and Year of Operation*

Lobe	Nodes	Operations			
		Pre-1953		All	
		No.	%	No.	%
Right upper	Free	26	65	31	65
	Involved ..	14	35	17	35
,, middle	Free	5	71	7	78
	Involved ..	2	29	2	22
,, lower	Free ..	39	72	53	75
	Involved ..	15	28	18	25
Main bronchus	Free	1	33	1	33
	Involved ..	2	67	2	67
Right lung	Free	72	68	92	70
	Involved ..	33	32	39	30
Left upper	Free	39	63	57	69
	Involved ..	23	37	26	31
,, lower	Free	25	52	32	51
	Involved ..	23	48	31	49
Main bronchus	Free	—	—	2	40
	Involved ..	2	100	3	60
Left lung	Free	64	57	91	60
	Involved ..	48	43	60	40

The proportions of each histological type of tumour showing nodal involvement increased every year up to and including 1953, with the exception of adenocarcinomas. Since their numbers are small and we have found them similar in other respects, they are best considered along with the undifferentiated tumours (Table VII), and this combined group showed the greater increase of nodal involvement. Prior to 1951 the incidence of nodal involvement in the combined group was 26%, compared with 23% for squamous tumours, but in 1953 it increased to 64%, compared with 36% for squamous types. While, therefore, nodal involvement in squamous tumours increased only from 23% to 36%, the combined group actually reached nearly twice this figure.

Why this should happen is not clear; the duration of symptoms was shorter each year, suggesting that the tumours were being operated on at an earlier stage (see below). It is unlikely to be due to keener histological search, since the incidence decreased in all instances in the last year (1954), and although it could have been due to acceptance of patients with greater clinical likelihood of nodal involvement followed by retrenchment in 1954, when results in 1953 were found to be less satisfactory (see above), this is very unlikely. No satisfactory explanation is therefore forthcoming.

Duration of Symptoms Prior to Operation

The expectation of survival did not, as might be first supposed, bear a direct relation to the period for which symptoms had been present at the time of operation.

Like Bignall and Moon (1955), we found the best chance of survival among those with longer histories (over nine months), which had two- and five-year rates of 59% and 33%. Those with histories of less than six months had intermediate rates of 46% and 30%, whilst for those with symptoms of six to nine months the rates were the worst at 36% and 19% respectively (Table IX).

TABLE IX.—*Duration of Symptoms Related to Histological Type of Tumour, Condition of Nodes, Two- and Five-year Survivors*

	Under 6 Months		6 to 9 Months		Over 9 Months	
	No.	%	No.	%	No.	%
5 years total ..	54		27		15	
Surviving ..	16	30	5	19	5	33
2 years total ..	183		50		27	
Surviving ..	85	46	18	36	16	59
Nodes free ..	94	63	19	61	14	64
,, involved ..	56	37	12	39	8	36
Squamous ..	87	59	12	41	14	67
Adenocarcinoma plus undifferentiated	60	41	17	59	7	33

Nodal involvement remained remarkably constant in relation to the length of history, so that this factor was not in this instance responsible for the influence on survival (Table IX). Contrary to Bignall's finding, however, in our series the percentage of squamous tumours in the groups paralleled the survival rates closely, and the six-to-nine-months group was the only one with more adenocarcinomas and undifferentiated tumours. Also unlike him, as already noted, we found that the effect of duration of symptoms was as great on the five-year rates as on the two-year.

The tumour site had a similar distribution among the under-six-months and six-to-nine-months groups, but with fewer left lower lobe tumours in the over-nine-months group. Hence site has no effect on the two shorter periods, but may have contributed a little to the improved chance of survival in the longest group.

It would appear from our series that the superior survival rates in the patients with long or short histories compared with the intermediate group is mainly due to the inclusion of more patients with squamous tumours (Table IX).

We agree with Bignall that patients coming to operation early stand a better chance of having the tumour removed before metastases have occurred and that those with long histories have slower-growing types of tumour, and we likewise found the incidence of metastases was highest in those with histories of intermediate length.

The average duration of symptoms for patients coming to operation in succeeding years showed a steady reduction (Table VII). In 1953 this was two and a half months, or 40% of the pre-1951 figure, probably due to earlier diagnosis and more expeditious handling on the part of the practitioner, aided by improved thoracic surgical services generally.

Despite the reduction of the duration of symptoms, the two-year survival rate for any given year remained constant around 45% (Table VII), whereas with earlier diagnosis it should have improved. The survival rate has not been affected either by variation in the average age of patients operated on or by the proportions of total and subtotal operations performed (Table VII), since, though the latter varied from year to year, the two-year survival rate is the same for both types of operation (Table V). A practical answer to this is that the proportion of patients with involved nodes increased steadily from 25% pre-1951 to 47% in 1953, but fell again to 27% in 1954. The significance of this cannot be appreciated, as at the time of this review in December, 1955, the two-year survival rate for the patients treated in 1954 could not be calculated.

A similar effect might have resulted from an increased proportion of the more malignant types of tumour, but Table VII shows that, though it fluctuated, the proportion actually fell from 50% in 1952 to 38% in 1953. To offset this, squamous tumours showed more evidence of metastases in 1952 and 1953 with over 30% involvement, compared with just over 20% in 1951 and earlier. In 1954 it was 24%.

It would thus appear that the advantage gained by early operation was offset by the annually increasing frequency of nodal metastases up to 1953.

Extent of Operation

The two-year survival rates after pneumonectomy and lobectomy were practically equal with 45% and 44% respectively. The five-year rates (Table V), however, differed considerably with 29% and 12.5%. Squamous tumours were found equally after both types of operation, but adenocarcinomas slightly more often after lobectomy, at the expense of undifferentiated types. This might be expected, since adenocarcinomas tend to be peripheral and circumscribed (Table VI).

Nodal involvement was found after 39% of pneumonectomies and 27% of lobectomies; and in patients surviving pneumonectomy or lobectomy for two years nodes were found to be involved in 38% and 33% respectively. Of the patients living five years after pneumonectomy, only 25% were found to have nodes involved originally. The survival rates after both operations were similar up to three years, but, later, patients who had undergone pneumonectomy survived better; and, knowing that all those dying of carcinoma after lobectomy did so within three years, we have the impression that some of these might have lived longer with a pneumonectomy if this had been functionally possible.

The ultimate fate after lobectomy and pneumonectomy would seem to depend on the surgeon's appraisement of nodal involvement, especially in lower lobe tumours. There is, of course, a clear difference in operative risk and mortality for the two operations.

Discussion

Apart from purely symptomatic measures, the two main methods of treating bronchial carcinoma are radiotherapy and surgical excision. Bignall (1956) showed that, of 207 patients with and without mediastinal nodes treated by radiotherapy, 29% survived one year and 8% survived two years. Of 463 patients who received no treatment, only 8% survived one year and 6% two years.

We have shown that in the Liverpool Region, of 448 patients treated surgically over a period of 14 years, 53% lived one year and 35% lived two years, notwithstanding the fact that 30% of the survivors of the operation were found to have metastases in mediastinal or hilar lymph nodes. There is little doubt that, at the moment, surgical excision is the method of choice.

We have already shown that the proportion of registered cases treated successfully by surgery increased from 1.6% to 13.9% in 10 years and that the two-year survival rate remains in the region of 44%; therefore, roughly 6.2% of all patients with carcinoma of the lung have a chance of living two years with existing standards of diagnosis and surgical treatment, irrespective of the duration of symptoms.

Belcher (1956) has already emphasized the need for a conservative approach to lung resection in carcinoma cases to preserve adequate lung function, even to the extent of performing palliative lobectomy in cases with poor pulmonary function. The latter type of operation reduced the two-year survival rate from 52% to 33%.

Study of our operative results shows that pneumonectomy is twice as lethal an operation as lobectomy and that on the right side is even more so than that on the left. Robinson *et al.* (1956) found, despite an overall younger age group, that in tuberculous patients 31% died after right pneumonectomy compared with 7% after left pneumonectomy. They noted

that resection on the right side for all types of operation was three times as lethal as on the left side. We felt the marked difference between the two sides was due solely to the relative volumes of the two lungs and to the subsequent effects of mediastinal displacement on the heart and remaining lung after right-sided resection.

Accepting the need for conservative resection, the problem at operation is how little lung can be removed and yet give a hope of a five-year cure ?

Provided the anatomical situation of the tumour makes lobectomy a reasonable operation, the decision between performing a total or a subtotal operation must depend on nodal involvement as assessed at the time of operation. The upper lobe tumours present less of a problem than lower lobe lesions in that those with mediastinal nodal involvement have already metastasized and pneumonectomy will be no more radical a procedure than lobectomy. Study of 21 patients who had upper lobectomy and died of metastases showed that with two exceptions all were dead within two years—that is, within the period when nodal metastases usually affect prognosis. There is no reason to believe that these would have survived any longer after pneumonectomy even if they survived the major operation.

Lower lobe tumours are more difficult, especially on the left side, where we found 50% with nodal involvement compared with 25% on the right. Of the patients dying of metastases after lower and middle lobectomies, 22 had tumours in the lower lobes and four in the middle lobe. All the latter died within 12 months, and with two exceptions all those who had lower lobectomies were dead within 23 months. They thus survived about the same length of time as the patients after upper lobectomy. It is conceivable that right pneumonectomy might save a few more patients with lower lobe tumours, but, in view of Rouvière's (1932) work on lymphatic drainage from the left lower lobe, it is doubtful whether left pneumonectomy would have eliminated metastases, particularly if the subcarinal nodes were involved. It would be good fortune if no cancer cells had passed through to the right side by the time the node showed involvement.

We found, despite the reduction in the duration of symptoms, that the two-year survival rate has remained constant, about 45%, and concluded that this was due to increasing nodal involvement, particularly by squamous tumours. The proportion of lobectomies performed since 1951 (except 1953) has been over 40%, and the fact that the two-year rate has remained steady despite an annual increase of nodal involvement suggests that adequate gland removal has been obtained with the less extensive operation in most cases. We feel, therefore, that when the site of tumour and nodal involvement permits of lobectomy this operation is preferable because it preserves lung function and usually provides an adequate removal of the tumour and attendant lymph nodes.

Summary

The fate of 2,156 patients suffering from bronchial carcinoma admitted to the Liverpool Thoracic Surgical Unit has been studied and related to the known cases registered by the Cancer Control Organization.

714 patients were explored and 464 tumours resected ; 448 patients were followed to death or survival for a minimum of one year.

347 survived the arbitrary operative phase and 45% and 28% survived for two and five years respectively.

The cause of operative deaths has been analysed and 62.37% found to be due to " cardio-pulmonary failure."

Right-sided operations were more lethal than left, especially for pneumonectomy, and more so when deaths were due to cardio-pulmonary failure.

The quinquennial age group 55 to 59 years made up 24% of all survivors ; they had the lowest mortality after pneumonectomy and had the best two-year and five-year survival rates of 53% and 45% respectively.

Patients with growths in the right lower lobes had the earliest symptoms, the lowest incidence of nodal involvement, and the best five-year survival rate for both squamous and undifferentiated tumours.

Left lower lobe tumours had the highest nodal involvement and the highest proportion of undifferentiated tumours, but the survival rate was similar to the left upper lobe.

Adenocarcinoma appeared to be the most malignant type of tumour, though nodal involvement was no higher than with undifferentiated types.

Despite earlier operation in relation to symptoms, the two-year survival rate has hardly changed, probably owing to the increasing incidence of nodal metastases.

We thank all members of the Liverpool Thoracic Surgical Unit for the use of their case notes; the medical practitioners for their co-operation; Drs. J. S. Fulton and M. A. Stewart, of the Cancer Control Organization, and Mr. F. Ronald Edwards and Dr. O. F. Thomas for their advice and criticism; Mr. G. Wilkins for the preparation of the figures; and Mrs. D. Anthony and Miss J. Peet for undertaking work outside their normal secretarial duties.

REFERENCES

Belcher, J. R. (1956). *Lancet*, **1**, 349.
Bignall, J. R. (1956). Ibid., **1**, 876.
—— and Moon, A. J. (1955). *Thorax*, **10**, 183.
Brock, R. C. (1948). *British Medical Journal*, **2**, 737.
—— and Whytehead, L. L. (1955). *Brit. J. Surg.*, **43**, 8.
Graham, Evarts A. (1947). *Ann. roy. Coll. Surg. Engl.*, **1**, 248.
Mason, G. A. (1949). *Lancet*, **2**, 587.
Rienhoff, W. F. (1947). *Ann. Surg.*, **125**, 541.
Robinson, J. L. Jones, J. C., Meyer, B. W., and Franklin, S. R. (1956). *Amer. Rev. Tuberc.*, 73, 690.
Rouvière, H. (1932). *Anatomie des lymphatiques de l'homme*. Masson, Paris.
Sellors, T. H. (1955). *British Medical Journal*, **1**, 445.
—— Cruickshank, G., and Billimoria, B. R. (1947). *Lancet*, **2**, 119.
Taylor, A. B., and Waterhouse, J. A. H. (1950). *Thorax*, **5**, 257.
Thomas, C. P. (1952). *Ann. roy. Coll. Surg. Engl.*, **11**, 205.

COMPRESSION OF MEDIAN NERVE IN CARPAL TUNNEL AND ITS RELATION TO ACROPARAESTHESIAE

BY

HUGH GARLAND, T.D., M.D., F.R.C.P.

J. P. P. BRADSHAW, M.D., M.R.C.P.

AND

J. M. P. CLARK, M.B.E., F.R.C.S.

From the Departments of Neurology and Orthopaedic Surgery, the General Infirmary at Leeds

The purpose of this paper, which is based on a study of 53 patients with acroparaesthesiae, is to present information concerning the diagnosis, prognosis, and treatment of this condition and to discuss its underlying mechanism.

Schultze (1893) introduced the term " acroparaesthesiae " to describe nocturnal attacks of pain and paraesthesiae that affect the hands of middle-aged women. Wilson (1913) reported the syndrome, often with partial thenar atrophy and objective sensory loss over the digits, in association with cervical rib. Walshe (1945), however, stated that muscular wasting does not occur and the objective sensory loss is exceptional, though when the pain and paraesthesiae are maximal there may be some blunting of cutaneous sensibility over the digits. The most constant feature was, he considered, tenderness over the extensor muscles of the fore-