

## PROGNOSIS FOR BRONCHIAL CARCINOMA\*

BY

A. BRIAN TAYLOR AND J. A. H. WATERHOUSE

Bronchial carcinoma is a mortal disease, occurring in England and Wales with a real increasing frequency. This paper is based on a study of 1,592 cases from the Cancer Follow-Up Department of the Birmingham United Hospitals from 1936 to 1948, inclusive; on 1,239 pneumonectomies done by English thoracic surgeons; and on the Registrar-General's published figures.

The disease occurs among men six times more often than among women, at an average age of 54 years. It lasts an average of 9.9 months, with symptoms for 4.4 months before the diagnosis is made, and death occurs in a further 5.5 months.

The early symptoms are often vague, and early diagnosis is occasionally baffling even with all ancillary methods.

Pneumonectomy is the treatment of choice, but is quite often not possible. Thus, in 11.4% the first symptoms indicated an extension beyond the lung. The operability rate at thoracotomy is good.

Pneumonectomy is developing from the experimental stage and we can now begin to assess results. In England the earlier years of this survey were occupied by war, and pneumonectomies were few. Operative mortality is dropping: deaths within three months of operation are 25.2%; and within one month, 20%. Detailed study of 313 pneumonectomies gives:

Survival for 1 year as	52.7%
"    "    2 years "	33.3%
"    "    3    "    "	23.9%
"    "    4    "    "	18.7%
"    "    5    "    "	13.7%

Seventy-five patients are recorded who have survived five years or more following pneumonectomy for carcinoma of the lung, and this survival rate confirms the late Tudor-Edwards' statement in a presidential address to the Thoracic Society (1945), that pneumonectomy should be carried out in every case where conditions permit.

### INCREASE IN LUNG CANCER IN ENGLAND AND WALES

The increase in numbers of cases of lung cancer in England and Wales has been apparent for some years, and Stocks (1947) states that over the last 30 years the mortality has increased very rapidly, both in absolute figures and as a proportion of all other cancer sites.

#### *Standardized Death Rate*

Males from 1.1 (1910) to 10.6 (1938)

Females from 0.7 (1910) to 2.5 (1938)

---

\* Based on a paper read by A. B. Taylor to the Thoracic Society in Oslo in August, 1949.

*Percentage Lung Cancer Mortality to All Sites*

Males from 1.5% (1916) to 7.9% (1935)

Females from 0.8% (1916) to 2.2% (1935)

The proportionate increase, being just over five times (males) is less striking than the absolute (nearly 10 times).

Similar increases, not usually so great, have been recorded for other countries. For instance, Springett (1950) has compared the figures of lung cancer mortality in Norway with those for England and Wales. In Table I (from Springett), where

TABLE I  
DEATHS FROM CANCER OF LUNG AS PERCENTAGE OF ALL CANCER DEATHS

Norway			England and Wales		
	F	M		F	M
1921-25	0.7	0.6	1921	0.7	1.7
1926-30	0.5	0.9	1926	0.9	2.4
1931-35	1.0	1.2	1931	1.7	4.9
1936-40	1.5	2.1	1936	2.4	8.3
1941-45	2.2	3.2	1941	3.3	12.7
1946	2.8	3.5	1946	3.9	17.9

five years' experience in Norway is set against one year's experience in England and Wales, it will be seen that in each country the male mortality is greater than that of the female, though in different proportions. Also, the female proportionate mortality figures for England and Wales compare very closely with the male figures for Norway at each period. From 1921 to 1946 in England and Wales, the male proportionate rate has shown a tenfold increase.

Jakobsen (personal communication) confirms the increase in Norway. In Denmark, Glemmesen and Busk (1947) have noted a rising crude mortality rate for lung cancer since 1931, especially in Copenhagen, their observation being based on Danish death certificates. They are still cautious, however, and think the apparent increase may be due to better diagnosis.

Stocks considers the increase in England is not due to better diagnosis or diagnostic facilities alone. In England and Wales, even over the 10-year period from 1938 to 1947 the crude mortality rate per million living has doubled (from 113 to 228, males and females together), and over the same period the average sex ratio (all ages) has increased from 3.7 to 1 (1938) to 5.1 to 1 (1947).

## SIGNIFICANT FACTORS IN DISTRIBUTION

Carcinoma of the lung is very variable in its incidence throughout the country.

*Urban-Rural.*—There is a steep downward grade of death rates at every age, from London through large and small towns to rural areas. No discernible trends are found with either social class or housing density.

*Sunshine.*—A marked variation (negatively) occurs with hours of sunshine. For 20 large county boroughs divided into three groups by their mean annual sunshine hours, the lung cancer mortality ratios (taking all county boroughs as 100) were:

*Hours' Sunshine*

Group I Under 1,150	.....	152
„ II 1,150-1,400	.....	100
„ III Over 1,400	.....	58

Stocks says:

“Either smokiness of atmosphere is an important factor in itself in producing lung cancer, or sunshine is an important factor in preventing its incidence.”

*Sea-Inland.*—If these same 20 county boroughs are divided into two groups, coastal towns and inland, the average ratios (to all country boroughs—100) are:

Sea	.....	66
Inland	.....	138

*Regional Differences.*—Bolton (mortality ratio=40) and Huddersfield (mortality ratio=243) are the most extreme towns in the sample. They are about the same latitude, not more than 30 miles from each other, and both manufacturing towns. They are situated on either side of the Pennines, so that possibly prevailing winds may exert a direct or indirect effect. Possibly cotton and wool show different occupational risks of lung cancer. Stocks records a large difference in rates for lung cancer between Lancashire county boroughs and West Riding county boroughs (excluding the very large towns), but can suggest no explanation. Nevertheless, regional differences in the mortality of lung cancer of this magnitude might well repay more detailed examination.

There can be little doubt, however, that geographical and occupational factors are of importance, and that changing habits or circumstances are related to a changing incidence of lung cancer as for many other diseases. The influence of conditions of life has long been known to play a part, as was shown among the Schneeberg miners. More recently Machle and Gregorius (1948) have investigated the incidence of the disease among workers in the chromate-producing industry in the United States. They found that the mortality of lung cancer in chromate workers over 50 was 40 times that for other comparable industrial groups, and that the mono-chromates appeared to be the carcinogenic hazard. The fact that the mean duration of exposure to risk was 14.5 years emphasizes the difficulties of attributing changing mortality rates directly to changing circumstances of life, whether in personal habits or in such things as composition of road surfaces. There may be a considerable latent period in the development of the disease, which would make the precise assessment of the contributing conditions a very difficult and tedious task.

The very wide variation in mortality rates of lung cancer both geographically and chronologically over a comparatively small range of distance and time indicates a pronounced environmental factor in its aetiology. The significance of this fact is that a detailed statistical investigation, taking into account all the principal differentials and sources of variation, should yield material invaluable in the elucidation of the aetiology and in the prevention of the disease—possibly of use also in diagnosis and treatment. In anticipation of any such statistical survey it may not be out of place to re-emphasize the necessity of recording every relevant detail for each case seen, including as complete a social and occupational history as possible.

THE BIRMINGHAM CASES

The Cancer Follow-Up Department of the United Birmingham Hospitals has recorded 1,592 cases between 1936 and 1948, and has traced every case except one till death, or, for the purpose of this investigation, till June, 1949. The scope of their survey has lately widened to include other Birmingham hospitals, and also centres associated with them in the Midlands.

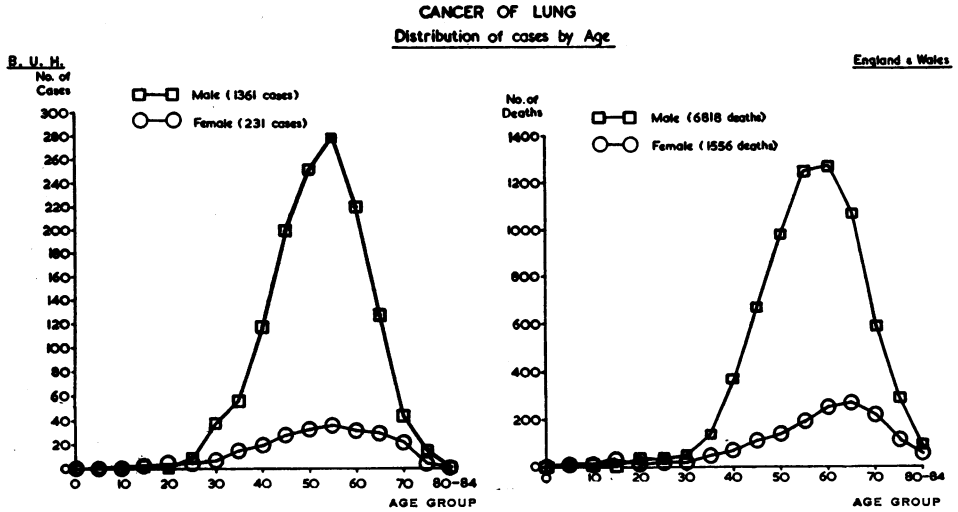


FIG. 1

Fig. 1 compares the age distribution of all United Birmingham Hospitals cases by sex with that of England and Wales. For the United Birmingham Hospitals

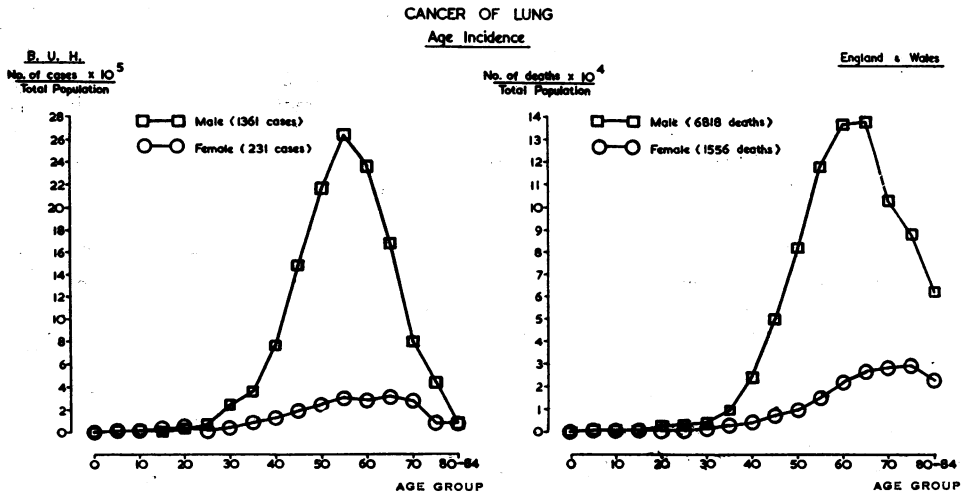


FIG. 2

cases the age is that when first seen, so that it represents a morbidity distribution ; the England and Wales figures refer to age at death, representing a mortality distribution. The comparison of morbidity with mortality is justified, however, in this example, as the average survival period is six months or under. Fig. 2 compares the age-incidence by sex for the same groups, on an arbitrary scale, showing the relative risk at any age of contracting the disease, when due allowance is made for the actual populations alive and at risk in the separate age and sex groups.

The Birmingham curves show earlier peaks than those for England and Wales : the difference in age is statistically significant but probably betokens nothing more than the occupational, climatic, and geographical differences between the Birmingham region and the country as a whole.

There is a general similarity of shape between the Birmingham and England and Wales curves in these as in Fig. 3, though the greater smoothness of the United Birmingham Hospitals curves compared with the angularity of those for England and Wales suggests not unreasonably that Birmingham constitutes a more homogeneous region than the country as a whole.

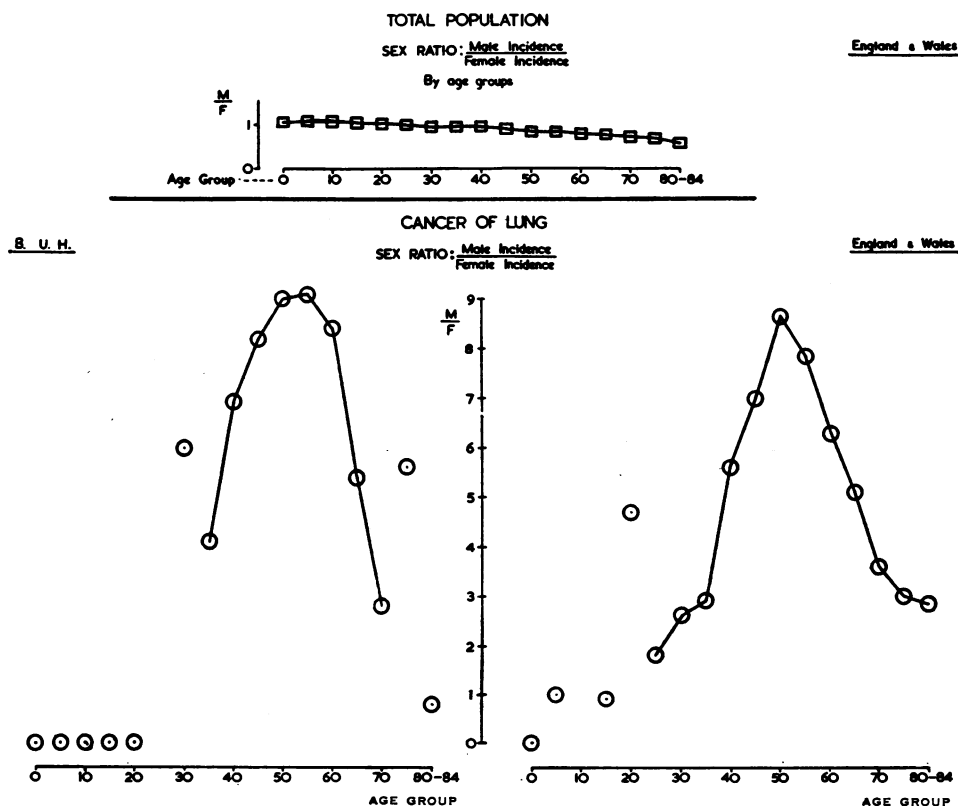


FIG. 3

Fig. 3 displays the comparative sex-ratios by age, again corrected to allow for the changing ratio in the general population. The maximum sex-ratio (about 9 : 1) occurs around the age of 55, slightly earlier for England and Wales, and later for United Birmingham Hospitals.

*Survival.*—Analysis of the 1,592 cases from the United Birmingham Hospitals shows a mean survival after diagnosis of 4.4 months. If 92 pneumonectomy cases are excluded, the survival is 4.0 months, the maximum being 43 months (only three cases more than three years), and the minimum 0 months (“brought in dead”).

The average duration of symptoms before diagnosis is 5.5 months, and thus in untreated cases the average duration of the disease to death is 9.9 months after the onset of recognizable symptoms, though we must accept the possibility that seeds of the disease are laid in early life.

Overholt and Schmidt (1949) analysed a series of cases in New England from 1932 to 1942, and found an average duration of symptoms before diagnosis of 11½ months, and in 1947–8 it was still 10 months, so that the problem of early diagnosis seems to be as difficult there

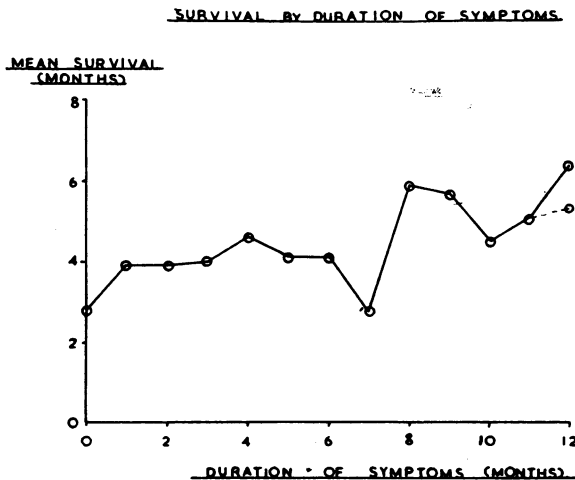


FIG. 4.

as in this country, due partly to the insidious nature of the early symptoms and failure of the patient to seek early medical advice, and also to procrastination by the general practitioner and failure to have radiological and other investigations early enough.

The relation of duration of symptoms to duration of life shows, interestingly, the variable rate of growth in different cases (Fig. 4).

With symptoms of 0 months, survival was 2.8 months
"    "    "    4    "    "    "    4.6    "
"    "    "    12   "    "    "    5.3    "

The relationship over this period of 12 months is just significant. Thus the importance of recognizing early symptoms cannot be overstressed. In our Birmingham cases the incidence of first symptoms was as in Table II.

In a consecutive group of 604 cases, haemoptysis was a symptom in 149, i.e., 24.7%. The disease is inoperable in more than 10% from its first recognizable symptoms. Thus of the quoted Birmingham cases, the first symptoms were:

Neurological	6.1%
Voice change (i.e., recurrent laryngeal paralysis)	1.8
Swelling of neck (i.e., vena-caval obstruction)	2.3
Superficial secondaries	0.5
Dysphagia	0.7
<b>Total</b>	<b>11.4%</b>

TABLE II

ANALYSIS OF FIRST SYMPTOMS BY TYPE (WHEREVER STATED) AT BIRMINGHAM UNITED HOSPITALS

Symptoms	Pneumonectomy		Other		Total	
	No.	%	No.	%	No.	%
Cough .. .. .	38	43.2	396	26.2	434	28.7
Pain .. .. .	11	12.5	321	21.2	332	21.9
Dyspnoea .. .. .	8	9.1	186	12.3	194	12.8
Haemoptysis .. .. .	15	17.0	101	6.7	116	7.7
Pneumonia .. .. .	2	2.3	38	2.5	40	2.6
Pleurisy .. .. .	3	3.4	28	1.8	31	2.0
Bronchitis .. .. .	6	6.8	37	2.4	43	2.8
Sickness and indigestion ..	—	—	31	2.0	31	2.0
Swelling (neck and throat)	—	—	35	2.3	35	2.3
Alteration of voice ..	1	1.1	27	1.8	28	1.8
Loss of weight .. .. .	—	—	18	1.2	18	1.2
Superficial secondary ..	—	—	8	0.5	8	0.5
Dysphagia .. .. .	1	1.1	9	0.6	10	0.7
Malaise .. .. .	—	—	37	2.4	37	2.4
Exhaustion .. .. .	—	—	9	0.6	9	0.6
Night sweats .. .. .	—	—	6	0.4	6	0.4
Tightness (chest and throat)	—	—	11	0.7	11	0.7
Neurological .. .. .	—	—	93	6.1	93	6.1
Other .. .. .	3	3.4	35	2.3	38	2.5

SURVIVAL IN RELATION TO TREATMENT

*Radiotherapy.*—The value of radiotherapy is difficult to assess, as so often only hopeless cases are referred and few series of radical treatments in early cases have been reported. Most observers seem to be doubtful of any curative value; the relief of superior vena-caval obstruction and some other symptoms may be dramatic, but the duration of life is not influenced.

Waldron Smithers (1948) is optimistic of the value of newer techniques by higher voltage, acceleration of particles, multiple beams of radiation, and rotation of the patient or beam. He reports two cases living more than seven years after treatment. Dobbie (1949) has described 59 cases treated radically with 11 alive for periods of nine months to six years. Recent figures of the Liverpool Radium Institute (personal communication) are as follows:

Average survival for 916 untreated cases .....7.6 months  
 " " " 190 treated radically by x-rays .....14.7 months

Shorvan (1947) reports 213 cases from Mount Vernon Hospital during 1942-6: 75 were too advanced for treatment; four were post-operative; 23 received pallia-

tive, and 111 radical, x-ray therapy. Of the last, 28 were still alive (16 more than six months, one surviving 36 months); and 83 were dead (half in six months, and none surviving more than 30 months). The average survival was 15½ months. These figures all indicate an improving trend in radiotherapy.

*Pneumonectomy.*—Surgical extirpation still seems to be the method of choice and the most likely to give permanently good results, both as regards removing the growth and for giving good function afterwards. It has become obvious that normal activities can be recovered after pneumonectomy.

Evarts Graham (1947) has described the steps leading to his first successful one-stage pneumonectomy in 1933, which led the way to the widespread practice of this operation. Figures have been published widely which have confirmed the possibility of cure by pneumonectomy for bronchial carcinoma.

In his Lister lecture Graham (1947) reported 229 total pneumonectomies for various diseases. Of 53 pneumonectomies for malignant tumours done before 1942, i.e., more than five years, 15 were alive and well (five years survival of 28%); 28 patients (53%) did not survive the operation, so that of the 25 who did, 60% were alive more than five years later.

Ochsner, DeBakey, and Dixon (1948) report 195 resections (190 for carcinoma). Their hospital deaths have fallen from 54.5% to 16.4%, and their subsequent figures show:

No. of Cases Operated					Survival Time	Survival Rate
181	..	..	..	..	6 months	99 (54.7%)
148	..	..	..	..	1 year	58 (59.2%)
108	..	..	..	..	2 years	28 (25.9%)
80	..	..	..	..	3 "	16 (20.0%)
50	..	..	..	..	4 "	12 (24.0%)
40	..	..	..	..	5 "	11 (27.5%)

Reinhoff (1947) reports 112 pneumonectomies with an operative mortality of 22.3%. Of the 87 survivors, 30 were dead in less than one year and 14 died within six years. Forty-three were still alive, of whom 16 had lived more than three years, and one was still living after 13 years. Of untreated cases, all were dead in an average period of five months after leaving hospital.

Adams (1948) reports 56 resections with eight deaths, the operative mortality falling from 14.3% for the total to 5% in the last 39. Of the 48 discharged, 31 lived more than one year. Of 17 operated on before 1941, six survived more than five years (35.3%).

In this country there have been several series of cases reported. The late Tudor Edwards' series (1946) was one of the earliest. He had done resection in 70 cases. Of 66 pneumonectomies, 34 patients were still alive, five more than five years after operation. Brock (1948) reports 101 resections, including 86 pneumonectomies, with an operative mortality of 18%. Twenty-five died of recurrence, 12 in the first six months. Fifty-five were alive and well, eight for more than five years. Sellors (1947 and 1948) reported resection in 130 cases of which 122 were



pneumonectomies. The mortality was 15%, 44% succumbed to recurrence, and 10 patients lived more than four years, and five more than five years. Mason (1948) has given a masterly review of 1,000 cases of bronchial carcinoma, for which he has done 202 pneumonectomies. Of these, 54 died within a month of operation, 68 later from metastases, and 18 from other causes. There are 62 survivors two months to seven years after operation ; five have lived more than five years.

To obtain a general picture of the results of English surgeons, we have collected figures from the main centres where pneumonectomy has become routine, and we have knowledge thus of 1,239 pneumonectomies (Table III). Analysis of figures from different centres is a little difficult, as varying details and standards have been

TABLE III  
ANALYSIS OF PNEUMONECTOMY CASES

Surgeon	Town	No. of Cases
P. R. Allison .. .. .	Leeds	74
Norman Barrett .. .. .	London	42
R. Belsey and J. E. G. Pearson .. .. .	Bristol	60
R. C. Brock .. .. .	London	133
J. T. Chesterman .. .. .	Sheffield	20
W. P. Cleland .. .. .	London	51
F. Ronald Edwards .. .. .	Liverpool	52
A. Tudor Edwards .. .. .	London	66
F. J. Sambrook Gowar .. .. .	London, R.N., and Aberdeen	25
G. A. Mason .. .. .	Newcastle	218
Frank Nicholson .. .. .	Manchester	41
Hugh Reid .. .. .	Liverpool	2
T. Holmes Sellors .. .. .	London	176
C. Price Thomas .. .. .	London	139
O. S. Tubbs .. .. .	London	48
	Total	1,147
BIRMINGHAM UNITED HOSPITALS		
H. H. Sampson } A. L. d'Abreu } J. Leigh Collis } R. Brain }		92
	Grand Total	1,239

used. It has been possible to separate 1,134 cases ; of these, 821 have been given with partial detail, and 313 with sufficient for detailed analysis.

Operative mortality is improving as surgeons and their teams become more experienced, and as physicians present them with more suitable and early cases. For instance, in the United Birmingham Hospitals, the operative (less than one month) mortality in 1939-40 was 33%, and in 1947-8 it was 15% ; for the detailed group (including United Birmingham Hospitals) it was 38% in 1939-40 and just under 20% in 1947-8. The figures for the whole period are shown in Table IV.

As a result of surgical treatment, the mean duration of the disease can be compared with its natural progress.

TABLE IV  
ANALYSIS OF OPERATIVE MORTALITY

	U.B.H. (92)	Detailed* Figures (313)	Whole Series (1,134)
Operative mortality:			
Within 1 month .. .. .	14.1%	22.7%	24.3%
Within 3 months .. .. .	33.7%	31.0%	
Mean survival (from operation):			
† Excluding hospital deaths (up to 3 months) ..	15.5 months	18.2 months	20.2 months
† Including all cases .. .. .	10.6	12.2	15.2
Still alive .. .. .	40.2%	38.0%	41.3%

\* Include U.B.H. figures. † Including all "still alive" cases.

*All Other Forms of Treatment (U.B.H.)*

Mean duration of disease from first symptom ..... 9.9 months

*Pneumonectomy (U.B.H.)*

Mean duration of disease from first symptom:

  All cases ..... 18.4 months

  Excluding hospital deaths (up to 3 months) .... 23.3 months

Finally, the five-year survival rate is 13.7%. We have obtained records of only 109 pneumonectomies done five or more years ago. At that time many thoracic surgeons were occupied by the exigencies of the war. Seventy-five cases have survived five years or more after pneumonectomy; 15 are alive at the time of reporting more than five years after their operation. These latter figures refer to all cases of which we have obtained records, but we cannot express the results in the form of a survival rate because we have no information about how many cases were originally operated on, of whom these were the survivors. Table V summarizes the survival rates for each year for those centres where detailed figures were available. In the fractions, the numerator refers to the actual number of survivors, the denominator to the number of cases who could have survived for the period in question.

TABLE V  
SURVIVAL RATES (PNEUMONECTOMY CASES)

1 Year	2 Years	3 Years	4 Years	5 Years
145/275 (52.7%)	55/165 (33.3%)	27/113 (23.9%)	17/91 (18.7%)	10/73 (13.7%)

SUMMARY

A statistical review is given of the frequency, distribution, and survival of bronchial carcinoma in England and Wales.

The analysis is based on a study of 1,592 cases from the Cancer Follow-Up Department of the Birmingham United Hospitals from 1936 to 1948, inclusive; on 1,239 pneumonectomies done by English thoracic surgeons; and on the Registrar-General's published figures.

The prognosis is considered statistically in relation to radiotherapy, pneumonectomy, and all other forms of treatment.

It is a pleasure to thank the surgeons listed in the paper for their kind co-operation in sending us their results of operation, and at the same time acknowledge the brilliant results of their skill which can give such hope to those afflicted by this fell disease. We also gratefully recognize the extensive and exhaustive researches of the Cancer Follow-up Department controlled by Miss Levi. We also wish to acknowledge a grant from the British Empire Cancer Campaign to the Department of Medical Statistics.

## REFERENCES

- Adams, R. J. (1948). *J. thorac. Surg.*, **17**, 306.  
Brock, R. C. (1948). *Brit. med. J.*, **2**, 737-739.  
Clemmesen, J., and Busk, T. (1947). *Brit. J. Cancer*, **1**, 253-259.  
Dobbie, J. L. (1944). *Brit. J. Radiol.*, **17**, 107.  
Edwards, A. Tudor (1946). *Thorax*, **1**, 1.  
Graham, Everts, A. (1947). Lister Lecture. *Ann. R. Coll. Surg. Engl.*, **1**, 248.  
Jakobsen. Personal communication.  
Liverpool Radium Institute. Personal communication.  
Machle, W., and Gregorius, F. (1948). *Publ. Hlth Rep., Wash.*, **63**, 1114.  
Mason, G. A. (1949). *Lancet*, **2**, 587.  
Ochsner, A., DeBakey, M. E., and Dixon, L. (1947). *Ann. Surg.*, **125**, 522.  
Overholt, R. H., and Schmidt, I. C. (1949). *New Engl. J. Med.*, **240**, 491.  
Reinhoff, W. F. (1947). *Ann. Surg.*, **125**, 541-565.  
Sellors, T. H., Cruickshank, G., and Billimoria, B. R. (1947). *Lancet*, **2**, 119.  
Shorvan, L. M. (1947). *Brit. J. Radiol.*, **20**, 445-449.  
Smithers, D. Waldron (1949). *Ann. R. Coll. Surg. Engl.*, **4**, 242.  
Springett, V. H. (1950). *Tidsskr. norske Laegeforen.* (In Press.)  
Stocks, P. (1947). Studies on Medical and Population Subjects, No. 1. "Regional and Local Differences in Cancer Death Rates." London.