A STATISTICAL SURVEY OF 1,063 CASES

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The Clinical Cancer Research Committee of the British Empire Cancer Campaign has registered 15,197 cases of cancer seen in the hospitals of the Administrative County of London between April 1, 1938, and September 3, 1939, of which 1,063 or 7 per cent. were diagnosed as neoplasms of the bronchi, lungs, pleurae or mediastinum. The latest year for which the Registrar General's detailed figures are available is 1937, from which we find for England and Wales 5.6 per cent. of all fatal cancer cases affected the lung. The London incidence is higher than that for the whole country, as will be explained later.

Sex

There were 871 males and 192 females, a ratio of 4.5 to 1. This is in accordance with the findings of other observers, both in this country and abroad. Seyfarth (1924) gives the ratio as 5.7 to 1 in 303 cases in Leipzig, Levy Simpson (1928) gives 4 to 1 for 139 cases in London, and at Brompton Hospital in Davidson's (1930) series the figures were 89 males to 18 females. This sex incidence is not confined to the lung, it is found also in cancer of the larynx and of the oesophagus. When the percentage incidence of cancer of the respiratory tract to that of all regions is examined in the two sexes, the difference is very striking. The table below shows the Registrar General's figures for 1937 for (1) England and Wales, (2) the Administrative County of London, and (3) the British Empire Cancer Campaign's figures for the Administrative County of London for 17 months from April 1, 1938, to September 3, 1939.

	Males	Per cent. of total cases	Females	Per cent. of total cases
England and Wales, 1937, all sites	32,189	—	34,802	—
England and Wales, 1937, lung and larynx	4,169	13.0	1,185	2.3
England and Wales, 1937, lung alone	2,930	9.0	823	3.4
Administrative County of London, 1937, all sites	3,601	—	3,719	—
Administrative County of London, 1937, lung and larynx	670	18.61	166	4.46
Administrative County of London, 1937, lung alone		Figures not available		
B.E.C.C. series, all sites	7,286	—	7,911	—
B.E.C.C. series, lung and larynx	1,284	17.6	304	3.8
B.E.C.C. series, lung alone	871	12.0	192	2.4

Geographical Distribution

The percentage site distribution varies widely between town and country as shown by the following extract from a table published by the Registrar General.

1937.	Per cent. of larynx and lung carcinoma to all cancer deaths	
	Male	Female
London, Administrative County	18.6	4.46
12 other large towns	16.0	3.7
England and Wales, excluding London	10.86	2.9
Wales (northern)	6.0	2.1
U.S.A. in same year	6.75	2.16

It has been noticed in the Registrar General's reports since 1904 that the rates of mortality from cancer, irrespective of the organ affected, increase with urbanisation, being greatest in London and least in the rural districts. This applies to the rates for both carcinoma of accessible and inaccessible sites. It is not possible to be certain how far this preponderance in the towns in the case of carcinoma of the lung is due to better facilities for radiological diagnosis and bronchoscopy, and how much is due to a higher incidence. Stocks (1936, 1937) makes a comparison of the male mortality from cancer of the larynx, lung and oesophagus in various large towns in 1921-30, expressed as the percentage of the actual deaths to the number expected if the standard mortality in all county boroughs had been operative at each age. Here are a few of his figures.

	<i>Larynx</i>	<i>Lung</i>	<i>Oesophagus</i>
Manchester and Salford	175	164	156
Nottingham	151	163	87
London	129	171	136
Sheffield	127	186	103
Bristol	83	64	77
Leeds	69	195	75

The figure for the lung for a group of unspecified Lancashire industrial towns was 52, and as examples of rural areas we may take Anglesey 17, Monmouth 26, Pembroke 36.

The diagnosis of cancer of the larynx does not present difficulties such as are met with in lung cancer, and in Stocks' opinion the occurrence of a similar geographical distribution of mortality from both carcinoma of the lung and of the larynx renders it likely that the variation is not due to varying facilities for diagnosis, but to a similarity in the extrinsic factors producing the disease.

Is Carcinoma of the lung increasing in frequency?

Kikuth (1925) surveyed 246 cases of primary carcinoma of the lung which came to autopsy at a Hamburg hospital from 1889-1923, and found that from constituting 1 per cent. of all carcinoma in 1887, they had risen to 9.5 per cent. in 1923, the total number of carcinomas showing no great increase. Hanf (1927) records an increase at the Charité Hospital, Berlin, from 3.7 per cent. of all cancer autopsies in 1903 to 7.9 per cent. in 1925, the total number of autopsies remaining much the same. The literature contains several series of autopsy records from Germany, all showing a sharp rise from about 2-3 per cent. of all cancers before 1920 to 6-7 per cent. by 1925-27. The figures from the U.S.A. (Hoffman, 1929) are expressed as death rates, and show a rise from 0.6 per 100,000 in 1914 to 1.9 per 100,000 in 1927. Duguid's (1927) figures for the Manchester Royal Infirmary show a rise from 1.58 per cent. of all autopsies in 1886-1890 to 2.5 per cent. in 1921-25, but the percentage of total cancer cases is not recorded. Bonser (1928-29) states that as far back as 1893-97, the percentage of intrathoracic to total cancer in the Leeds series of autopsies was 7 per cent. The Registrar General's figures for deaths from carcinoma of the respiratory tract for 1928 and 1938 are as follows:—

	1928		1938	
Total cancer deaths	Male	26,013	Male	32,692
	Female	30,240	Female	35,193
Deaths from respiratory cancer	Male	1,984 = 7.6 per cent.	Male	4,580 = 14.0 per cent.
	Female	708 = 2.3 per cent.	Female	1,340 = 3.7 per cent.

Whilst the total number of cancer deaths in both sexes combined has risen by 22 per cent., that for respiratory cancer has risen by 120 per cent. The Registrar General gives the standardised mortality for cancer of the lung (separated from the figures for the larynx) as:—

	1921-30	1937
Males	25.1 per million	100.9 per million
Females	9.6 per million	23.2 per million

The figures for carcinoma of the larynx show a slight fall in both sexes over the same period. Whilst these figures appear to show a steady increase in the mortality from cancer of the lung, it may be that this increase is more apparent than real due to improved methods of diagnosis and the increased attention paid to this condition in recent years. The B.E.C.C. figures of course provide no evidence on the point, as they cover too short a period, but in course of time it is hoped that valuable material for the solution of this and similar problems may be collected.

Age Incidence

The cases have been divided into four groups according to the probable site of origin.

A. Trachea	7 cases, all males
B. Bronchi, lungs, pleuræ	1,023 cases, 841 males 182 females
C. Mediastinum	29 cases, 19 males 10 females
D. Thyms	4 cases, all males

The age incidence of group B was as follows:—

	<i>Males</i>	<i>Females</i>	<i>Total</i>
15-24	7	3	10
25-34	20	6	26
35-39	26	8	34
40-44	69	13	82
45-49	101	17	118
50-54	148	17	165
55-59	158	30	188
60-64	147	34	181
65-69	104	22	126
70-74	40	15	55
75-79	14	12	26
80-84	4	5	9
Over 85	1	—	1
Not stated	2	—	2

	<i>Males</i>	<i>Females</i>
Total	841	182
Mean age	55.90 $\pm$.39	57.7 $\pm$ 1.05
Standard deviation	11.15 $\pm$ 0.27	14.2 $\pm$ 0.7

The peak period is in the 55-60 group for males and in the 60-65 group for females. The difference between the mean ages for males and females, 1.8 years, is not statistically significant.

Heredity

A history of cancer in parents or siblings was obtained in 8 per cent. of the male patients and 14 per cent. of the females. As the percentage of cases in which information on this point was not obtained was 33 and 31 per cent. respectively, the margins of error are too wide to permit of any inference being drawn from the figures.

Aetiology

Occupation.—Kennaway (1936) classified the occupations of 18,280 persons dying from carcinoma of the respiratory tract for the years 1921-32. He found that in all occupations where there is exposure to road dust (paviours, road sweepers, horse and motor drivers) there is a high incidence of carcinoma of the lung. Most dusty occupations show no great frequency, with the exception of metal grinders, who are liable to fibrosis of the lung from silica dust, and in them the frequency of lung carcinoma is 2½ times normal. Available data suggest coal tar, whether from road, chimney, or any other source, does not cause carcinoma of the lung; it is noteworthy that cotton mule spinners have an especially small liability, though they inhale air sprayed with carcinogenic oil. The often quoted high incidence of pulmonary cancer amongst the Schneeberg miners has been variously attributed to arsenic and cobalt, to particles of quartz mixed with steel which are sprayed into the workers' faces by the cutting tools and to radio-activity, which is said to be responsible for a high incidence of pulmonary carcinoma in the radium mines in Czechoslovakia. Clinically the cases presented the symptoms and signs of pneumoconiosis for some years before the presence of a tumour was detected by X-rays.

The occupations of 871 male cases were tabulated and the most common were found to be:

General and dock labourer	102
Engineers, mechanics, fitters	47
Painters, decorators, paperhangers	42
Motor drivers	36
Clerks	35
Barmen, brewers and waiters	19
Builders and bricklayers	16
None (mostly old age pensioners and previous occupations not stated)	148

In occupations involving much inhalation of dust, there were 4 coalminers, 4 grinders, 3 chimney sweeps and 2 horse transport drivers. Agricultural work was represented by 7 gardeners and 6 farmers or farm labourers, and workers in gasworks by 5. In the absence of control figures of the occupations of all patients attending London hospitals, it is impossible

to say whether these figures show any significant deviation from the average. 80 per cent. of the patients were town dwellers and 18 per cent. lived in the country.

Tobacco.—The percentage of smokers was estimated in a group of 69 men and 18 women, mostly from one hospital. Of the men 4.3 per cent. were non-smokers, 26.1 per cent. moderate, and 40.5 per cent. excessive smokers (over 3 ozs. of tobacco per week), with 29 per cent. not stated. Of the women, one-third were non-smokers, one-third not stated, and the remaining third were moderate smokers.

Previous Respiratory Diseases.—There were 42 cases (4.1 per cent.) with a history of proved tuberculosis, 21 of which were pulmonary, 712 (69.6 per cent.) definite negatives, and 270 (26.3 per cent.) not stated. There was a history of pneumonia in 127 (12.4 per cent.) cases, and of influenza in 165 (16.1 per cent.) in 15 of which there was definite broncho-pneumonia, but the interval between the acute attack and the onset of symptoms of carcinoma is not stated. A history of chronic bronchitis was recorded in 273 cases (27 per cent.), of bronchiectasis in 20 (2 per cent.), and of pneumoconiosis in 1 case only. There was a history of syphilis in 18 cases, all males, and 15 cases were found to have a positive Wassermann out of 212 in which this was tested. In all these groups the percentage of cases in which the question was not answered was 26–33, and, before drawing deductions, the figures require to be compared with control figures taken from the general population of the same age groups.

First Symptom

Arranged in order of frequency, the first symptom was:—

	Cases	Per cent.
Cough	329	32.1
Pain in chest	190	18.5
Symptoms of pleurisy or intrathoracic infection	95	9.3
Dyspnoea	92	9.0
General asthenia	90	8.8
Haemoptysis	89	8.7
Symptoms due to metastases	71	6.9
Discovered on examination or at P.M.	23	2.2
Dysphagia or regurgitation	18	1.8
Hoarseness and other symptoms	15	1.5
Pressure symptoms	12	1.2

The groups in which onset resembles an attack of pleurisy or is with haemoptysis or a gradually increasing asthenia are likely to lead to mistaken diagnoses. The 71 cases in which symptoms due to metastases were the first noticed, includes 18 of metastases in the brain (4 of them were diagnosed as cerebral tumours until the P.M. revealed the primary).

Interval from First Symptom to First Consultation

The serious character of the symptoms and the rapid progress of the disease led to medical advice being sought early, and we find that 46 per cent. of the patients consulted a doctor within one month and 64 per cent. within the first three months. In 21 per cent. of the cases it was impossible to determine the interval as the patients had complained of a chronic cough for years.

Condition on Admission to Hospital

Good	101	Bad	108
Fair	304	Moribund	64
Poor	415	Not stated	31

Localisation.—96.1 per cent. of cases were classified as arising from a bronchus, in 2.9 per cent. the site of origin could not be exactly defined, and the remaining 1 per cent. were growths of the pleura. 51.2 per cent. arose on the right side, 46.5 per cent. on the left, and the remaining 2.3 per cent. were central or bilateral. Most observers find this preponderance of the right over the left side, which they explain on anatomical grounds.

Some physical signs.—Enlarged supraclavicular lymph nodes were found in 16 per cent. and enlarged cervical or axillary nodes in 13 per cent. (with 10–13 per cent. "not stated"). Dilated veins were present in 14 per cent. (19 per cent. "not stated"), osteoarthropathy in 20 per cent. (20 per cent. "not stated"), Horner's syndrome in 2.6 per cent. (24 per cent. "not stated") and signs of bronchial obstruction in 52 per cent. (18 per cent. "not stated").

Sputum Examination.—In 263 cases the sputum was examined for carcinoma cells, with positive results in 71 (27 per cent.).

X-ray Findings.—An X-ray of the chest was done in 86 per cent. of the cases. The findings briefly summarised were: localised opacity in 24 per cent., opacity of a whole lobe or lung in 20 per cent., collapse in 17 per cent., hilar masses in 14 per cent., a pleural effusion in 13 per cent., and some other sign in 12 per cent. X-ray examination, after lipiodol injection, was done in 154 cases, and definite bronchial obstruction was demonstrated in 135 cases.

Bronchoscopy.—This was done in 329 (about one-third) of the cases. Of these nothing abnormal was seen in 11 per cent., a definite neoplasm in 59 per cent., bronchial obstruction including that due to external pressure, in 36 per cent., and indefinite findings in 3 per cent.

Remote Metastases.—These were detected clinically or radiologically in 249 (24.3 per cent.) cases, and were distributed as follows:—

Liver and abdominal organs	83
Skull, spine, ribs and sternum	56
Lungs, pleurae or other thoracic organs	44
Brain	42
Bones of extremities	25
Skin and subcutaneous	24
Lymph nodes, other than cervical, axillary or mediastinal	10
Bones of pelvis	11
Upper respiratory tract	3

In 28 cases the metastases were multiple. If operation findings, with P.M. findings in cases admitted moribund, are taken into consideration the number rises to 361 cases in this group.

Staging.—The cases may be roughly classified into three groups on the clinical and operation findings:—

I. Growth confined to organ of origin	325 (31.8 per cent.)
II. Regional, supraclavicular or cervical nodes involved, or apparently spreading to neighbouring tissues	325 (31.8 per cent.)
III. Remote metastases present	361 (35.2 per cent.)
Unstaged	12 (1.2 per cent.)

Treatment. 15 cases (9 stage I and 6 stage II) were treated by pneumonectomy. The operation mortality was 8 (53 per cent.), 5 from shock, 2 from pneumonia, and 1 from pulmonary embolism. 4 died in the first year, 1 is alive at 2 years, 2 are untraced. A transthoracic exploration was done in 32 cases, of whom 12 had radiotherapy in addition. The operation mortality was 7 (23.3 per cent.).

203 cases were treated by deep X-rays alone, 37 by intrapulmonary radon, 3 by combinations of X-rays with radon, and 6 by deep X-rays combined with palliative surgical procedures. 109 cases were treated by palliative surgical procedures only, such as aspiration of fluid or rib resection, and in 15 cases a metastasis was operated upon under the impression that it was the primary. In 586 cases (57 per cent.) no active treatment was practicable.

Histological Examination.

Biopsy was performed in 33 per cent. of the cases, in only 10 per cent. of which it failed to confirm the clinical diagnosis of malignancy. Histological examination was made in 651 cases (63.6 per cent.) with the following results:—

Specimen was not malignant	58	Adenocarcinoma	49
Specimen was doubtful	18	Spheroidal cell carcinoma	70
Carcinoma	85	"Oat" cell carcinoma	198
Endothelioma	3	Reticulum cell sarcoma	2
Squamous cell carcinoma	158	Leiomyosarcoma	1
Transitional cell carcinoma	8		
Basal cell carcinoma	1		

Results—2 year follow-up

Died in 1st year	937	Total deaths	956
Died in 2nd year	19	Total living	18
Alive at end of 2nd year	18	Total untraced	49
Untraced	49		
			1,023

Duration

The duration of the disease, calculated from the patient's statements of the dates of the first symptom was ascertained in 839 cases. The average was 9.0 ± 0.5 months, with a standard deviation of 7.5 months, 25 per cent. died within 3.5 months, 50 per cent. within 6.5 month and 75 per cent. within 11.6 months.

Autopsy

Autopsy was obtained in 46.5 per cent. of fatal cases. Death was attributed to cachexia in 64 per cent., to pulmonary complications in 19 per cent., and to haemorrhage in 2.4 per cent. The diagnosis was first made at the P.M. in 76 cases.

The Other Groups

Considerations of space render it impossible to deal with the other groups in detail. The 7 tracheal cases were at or just above the bifurcation in 3 cases. Of the 29 mediastinal neoplasm cases, the diagnosis was definitely proved in 12, probable in 10, and doubtful in 7 cases. The 4 thymus cases included two patients of 12 and 24 years of age respectively, and the diagnosis was verified pathologically in 2 cases.

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PATHOLOGY

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As far as human pathology is concerned primary carcinoma of the lung is limited to carcinoma of the bronchi and bronchioles. There is good reason for believing that the alveoli of normal human lungs have no continuous epithelial lining and that the scattered cuboidal cells found in them are really mesenchymal not epithelial in origin.¹

DEVELOPMENT AND SITES

Carcinomata arise most frequently in the main bronchi and their primary divisions, less commonly in the rest of the bronchial tree. The right bronchus is affected rather more commonly than the left. From examinations of the earliest growths it would appear that they most frequently arise at the junction of a bronchial branch with its parent stem. At first the mucosa over the growth is intact and in some cases it remains so to the end. The presence of an early carcinoma is shown by changes in colour, the bronchial mucosa over it being white, greyish-white or pink; often there is a central pale area surrounded by an irregular zone of increased vascularity. The carcinoma usually spreads both up and down the bronchial wall and also round it, some growths form polypous masses which fill or partly fill the lumen. On section the cut surface of the squamous celled growths is usually flat, granular and white with

¹ Barnard & T. D. Day, *Journ. Path. & Bact.* 1937, Vol. XIV, No. 1, pp. 67-83.