

Lung Cancer

Surgery and
Survival

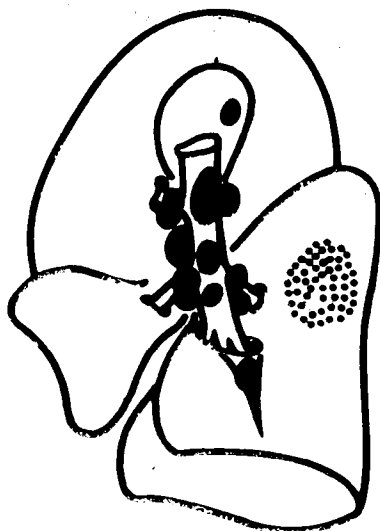
JOHN BORRIE



Lung Cancer

Surgery and Survival

by JOHN BORRIE



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To my teachers in Thoracic Surgery

PHILIP ALLISON

who in 1947 at Leeds first showed me the
possibilities of this method of studying lung
cancer

GEORGE A. MASON

who from 1948 to 1951 at Newcastle-upon-
Tyne gave me the opportunity and contin-
ued encouragement to undertake this work

To both I am profoundly grateful.

Preface

This detailed analysis of the anatomy, pathology, and clinical behavior of carcinoma of the lung, based on 200 surgical resections between 1941 and 1950, was largely undertaken between June, 1948, and October, 1951, when I was assistant Thoracic Surgeon at the North Regional Thoracic Surgical Centre, Newcastle-upon-Tyne, England.

The work was originally presented as a Hunterian Professorial Lecture in the Royal College of Surgeons, London, on October 4, 1951, and it was assembled in an extended form as a thesis a year later.

In the earlier analysis of 1951 I was able to emphasize the anatomic site and pathologic state of the lymph nodes of lungs excised for carcinoma of the lung and to indicate probable clinical behavior after operation. It was appreciated then, however, that a ten-year interval must elapse before total assessment was possible and before many related problems could be answered.

In 1961, during a period of sabbatical leave, an opportunity came to revisit Newcastle-upon-Tyne, England, and to complete a ten or more year follow-up on all of the 200 patients originally investigated.

Thus, the purpose of this book is to bring together all aspects of the work and to publish these as a monograph in a way that was not possible in my earlier articles in medical journals.

The details of the method of study, the dissection plan, the charting of each lymph node, its histologic examination, the making of a free-hand pen and ink sketch of each specimen, and the follow-up of the patients are told in Chapter 1.

This book, which is a study of the anatomy of the intrapulmonary lymph nodes and the behavior patterns of carcinoma of the lung, is based on that work. The charts of each patient, completed in the light of the ten-year follow-up, have been assembled and printed as far as is practicable to show how they are originally analyzed. Thereby, the reader himself is able to assess critically any conclusion drawn, including the anatomic sites of the intrapulmonary lymph nodes, as well as to observe the behavior of carcinoma of the lung in relation to lymph node invasion, survival time, and other related problems. The charts tell their own story far better than the written word.

This is essentially a study of "Carcinoma of the lung at the time the disease can still be resected," and I trust it may prove of value to physicians, surgeons, and pathologists alike. The section on the intrapulmonary lymph nodes may also interest anatomists.

One of the advantages of returning to a work after ten years is that, by returning to something long since put away but not forgotten, one has a fine opportunity to check one's own work with fresh critical eyes and to recheck all facts and figures.

Thus, there have been minor adjustments to some numbers in the earlier summarized publications. These, however, do *not* in any way alter the over-all picture already described.

The majority of the lung resections were done by Mr. G. A. Mason, but others contributing were Mr. S. G. Griffen, Mr. W. C. Barnsley, Mr. C. J. Evans, Mr. A. Simpson, and the author. The postoperative radiotherapy regime was supervised by Mr. C. J. L. Thurgar and Dr. W. Ross.

The consultant pathologists were Dr. E. K. Dawson, Dr. W. Lees, and Dr. J. D. McGregor of the Pathology Research Laboratory of the Royal College of Physicians of Edinburgh.

The compiling of this work, even in its original thesis format, was a considerable undertaking, to the expenses of which the Auckland, New Zealand, Division of the British Empire Cancer Campaign Soc. (Inc.) in 1952 made a generous donation. Mr. Litherland at that stage gave valuable photographic assistance.

The follow-up study, ten years later, was undertaken while on study-leave with a grant to cover expenses of a detour to Newcastle-upon-Tyne, from the Otago Division of the British Empire Cancer Soc. (Inc.), to whose practical encouragement I am most grateful.

The Newcastle Regional Hospital Board Cancer organization, under the general direction of Mr. C. J. L. Thurgar, is most fortunate in having on its staff Mr. N. C. Haynes, who not only helped me during my short return visit but has since then patiently answered all my questions and faithfully followed up all the patients from their hearths, if alive, to the records of Registrar-General of England if dead. Thanks to Mr. Haynes, I am able to present a 100 per cent follow-up of the patients.

In preparing this work for publication, it was necessary for me to redraw all the lung charts. I am most grateful to Miss Leoni Duncan for her assistance in this task and for her lettering of these charts. I thank also Mr. Gerald Brook for his photographic advice, and Mr. Brian Connor and Donald Weston for copying and duplicating all the charts and diagrams. All are members of the Medical Illustration Department, Medical School, University of Otago.

I also thank my Thoracic Surgical colleague, Mr. Ivan Lichter, F.R.C.S., for his helpful criticism of the manuscript.

I owe special thanks to Mr. H. D. Erlam, Medical School Librarian, for his painstaking reading of the manuscript and his many helpful suggestions.

Miss F. Pickin of the Medical Library, University of Otago, gave great assistance in verifying the references.

I gratefully acknowledge the devoted and untiring services of my secretary, Miss L. Thompson, and also the help of Mrs. Q. Stuart with the final typing.

Finally I deeply appreciate the help, co-operation, and encouragement of the publisher.

JOHN BORRIE

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1

General Observations

Much is known of the nature of lung cancer, both clinically and pathologically. Its incidence has risen spectacularly until it has become the most common cancer in heavy-smoking males. Its presentation, its clinical course, and the variations in its final autopsy patterns are all well recognized.

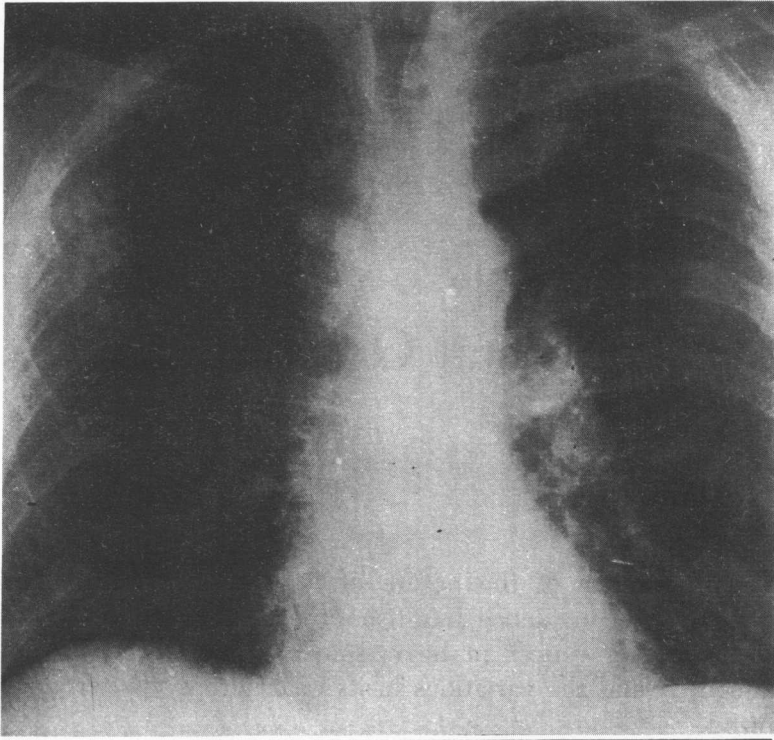
Because lung cancer carries off so many young men in their forties and fifties when they are still active, useful citizens, its early recognition and successful treatment are of the greatest importance. Its ultimate conquest and prevention, however, must wait until man changes his habits and way of life (1).

It is fair to say that for two thirds of the patients discovered to have carcinoma of the lung, treatment at present is still palliative and medical, designed to ease suffering and to allow them to die comfortably. In only a third of the patients is surgical treatment possible.

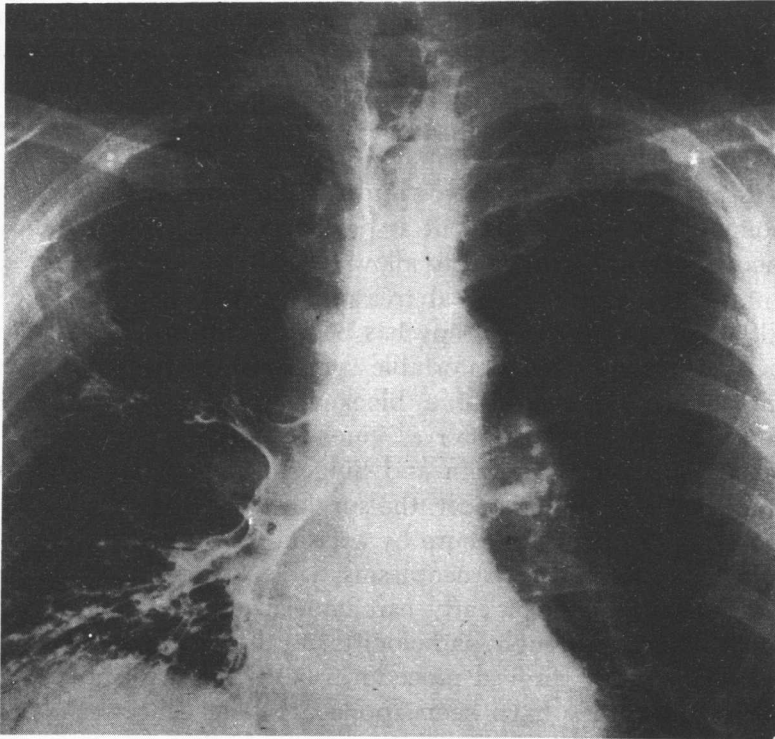
Although deep x-ray therapy has been shown to greatly relieve some inoperable patients of uncomfortable symptoms, such as pain, vena caval obstruction, or the effects of a blocked bronchus, it rarely effects an apparent cure. It does not offer as much as surgery.

Since 1933, when Graham and Singer (2) first described successful pneumonectomy for lung cancer, the surgical world has resolutely attacked the problem. Their quest to cure by excising the tumor has been fortified by high hopes that isolated neoplasms, when widely excised, should not recur and that surgery of early carcinomas is essentially surgery of the lymphatic system. Though pathologists in the past have been sceptical of these dicta, many surgical procedures have necessarily been built upon them. Naturally, they have been applied to lung cancer.

The general trend of the earlier papers (2-17) on surgery and lung cancer—especially the pioneering work of Macewan (3), Lilienthal (4),



A



B

Fig. 1. Man, aged 46. A. Chance x-ray showed right upper lobar shadow on 7/10/59. B. Bronchogram of 7/21/59 confirmed lesion and hilar lymph node enlargement. This proved inoperable. The patient died four weeks after diagnosis from rapidly growing undifferentiated carcinoma causing mediastinal compression.

Mason (5, 6), and Crafoord (7)—emphasized the technical problems of lung resection. By the late 1940's the results on various series of patients were being described by Edwards (8), Brock (9, 10, 11), Sweet (12), Rienhoff (13), and Ochsner and De Bakey (14), the technique of dissection pneumonectomy by Sellors (15, 16), and its refinement of intrapericardial dissection by Allison (17).

The detailed analysis of specimens excised surgically and their relation to the problems of prognosis and survival time was commenced by this writer (18, 19) in 1948 on 200 operation specimens. Nohl (20) in 1956 carried out a parallel and unrelated study. In his monograph of 1962 (21) on the spread of carcinoma of the bronchus, he emphasized the importance of the intrapulmonary lymphatic pathways. Furthermore, carrying his histologic studies into the venous system of the lung, he set out a surgical pathologic classification—based on five-year survivals—that should prove to be a real step forward in assessing prognosis after operation.

Certainly, this problem of prognosis has awaited a final solution since the first pneumonectomy for carcinoma of the lung in 1933. A number of questions remain unanswered: How does surgery affect the behavior of carcinoma of the lung? How long can patients expect to live after operation? Since man will not stop smoking, what is the most favorable age group for the development of lung cancer, what is the most favorable lung segment, and the most favorable cell-type of tumor?

VARIABLES IN LUNG CANCER

We now know that carcinoma of the lung as a lesion has many variables affecting a large range of patients. It may arise in any segment of the lung and is often far advanced when first assessed. It varies in its behavior from a "galloping" type that can run its course within a month (Figs. 1 and 2) to a round almost benign lesion that can remain in the lung for over a year and, when resected apparently late in its "cancer life," still allow the patient to be fit and well for five or more additional years (Figs. 3 and 4).

Even now diagnosis presents difficulties. For example, although in 1960-1961 17 of 55 patients with "positive" mass miniature x-ray films in the Southern Metropolitan Thoracic Surgical Unit in Dunedin, New Zealand, proved on resection to have lung cancer, there were during the same period ten patients with lung cancer whose chest films were normal or near normal. The disturbing inference is clear: Chest films are *not* infallible, and the need for sputum cytology and bronchoscopy studies is *not* excluded by a negative film in any patient who has symptoms relating to his lungs.

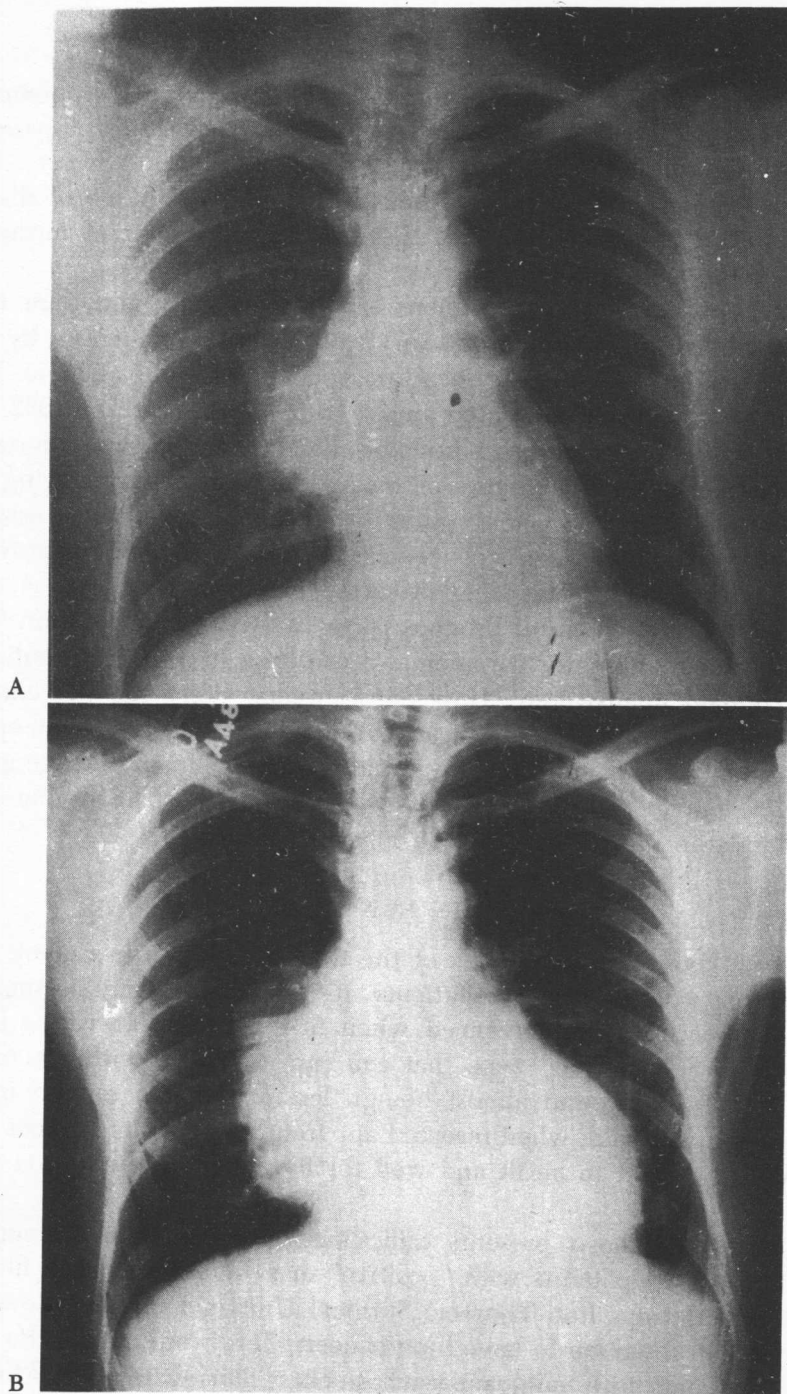
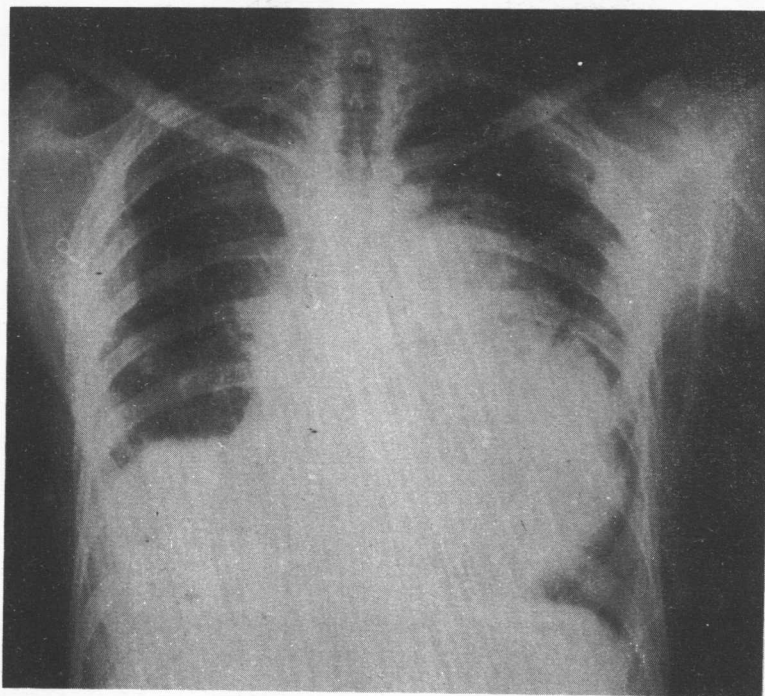


Fig. 2. Man, aged 29. Undifferentiated carcinoma of lung. A. Film of 7/18/57. Note tumor in right lung. B. Film of 7/30/57. Note rapid extension in 12 days. Right middle and lower lobectomy 8/1/57.



C

Fig. 2. C. Film of 9/9/57. Note gross mediastinal and left pulmonary recurrence. Death 10/12/57, three months after diagnosis of disease.

INCREASING INCIDENCE OF LUNG CANCER

The incidence of lung cancer continues to rise. Even in the 2.5 million population of New Zealand, it is now a national problem, thus following the pattern set in the Northern Hemisphere. In 1948 81 males in New Zealand died from lung cancer, as against 229 males who died from carcinoma of the stomach. By 1958 the rate had risen steeply, to 330 male deaths from lung cancer, as against 261 from stomach cancer. Lung cancer surpassed stomach cancer during 1953-1954, and by 1960 it had continued to soar, causing 398 male cancer deaths—that is, almost five times the rate for 1948 (22).

PROBLEMS RELATING TO SURGICAL TREATMENT

The problems posed include:

1. the anatomic sites of the intrapulmonary lymph nodes;
2. the usual pathway of lymphatic spread of carcinoma of the lung from the various lobes toward the hilum;

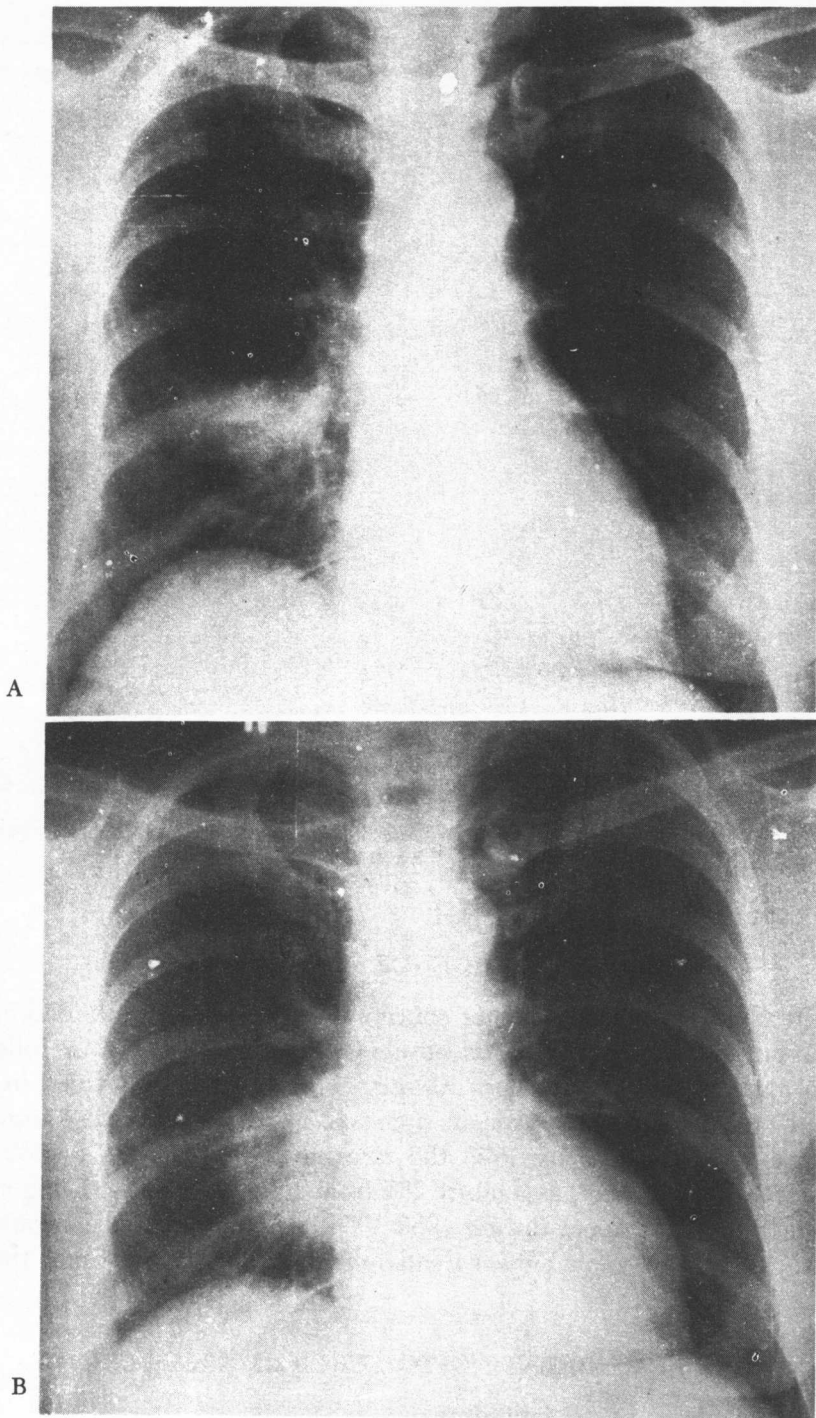


Fig. 3. Nonsmoking woman, aged 67. A. Film of 9/26/55. Tumor visible but not appreciated. Patient not referred. B. Film of 9/26/56. Tumor larger. Referred for treatment in 1956, after a year of diagnostic delay. She had right middle and lower lobectomies for adenocarcinoma of lung. Eight years later (9/26/64), she remains alive and well.

3. the nature and extent of pulmonary lymph node invasion at the time of operation;
4. the behavior of the various histologic types of carcinoma of lung with reference to the pulmonary lymph nodes;
5. the relationship of lymph node invasion to prognosis;
6. the relationship between site of growth and survival time;
7. the relationship between type of growth and survival time;
8. the effect of deep radiotherapy to the mediastinum after pneumonectomy (5000 r given by a 250-kv machine);
9. the relationship between the symptomless characteristics of a carcinoma of lung first detected by mass radiography and both extent of lymph node invasion and survival times;
10. the relationship, if any, between neoplastic invasion of the bronchus at the line of bronchial section and the subsequent development of postoperative bronchial fistulas;
11. the more usual causes of postoperative deaths.

THE MATERIAL AND ITS INVESTIGATION

Between 1933 and April, 1951, 1,800 patients with primary carcinoma of the lung were investigated in the North Regional Thoracic Surgical Centre, Newcastle-upon-Tyne, England. Of these, 45 per cent received operative treatment. In 26 per cent the growths could not be removed and thoracotomies alone was performed. In the remaining 19 per cent the lungs were resected.

THE SPECIMENS

Many of the original operation specimens covering the period 1941-1948 had been inflated with 10 per cent formalin solution and stored. They were thus available for dissections, which were carried out between July, 1948, and March, 1951. In addition, all specimens of carcinoma of the lung resected during the period 1948-1950 were studied. The total in both groups was 200 specimens.

After formalin inflation and fixation, each specimen was cut, and its macroscopic features were recorded in a pen and ink drawing of the lung or lobe. Next, the growth was histologically examined, as was a circle of its main bronchus at the line of surgical division. In selected cases the veins in the specimens were examined macroscopically and microscopically for evidence of tumor invasion.

The site of each lymph node in the specimen was charted in relation to the anatomy of the bronchial tree. The node was then excised, serially numbered, and histologically examined. If found to be invaded by growth, a drawing of the node was completed in black ink.

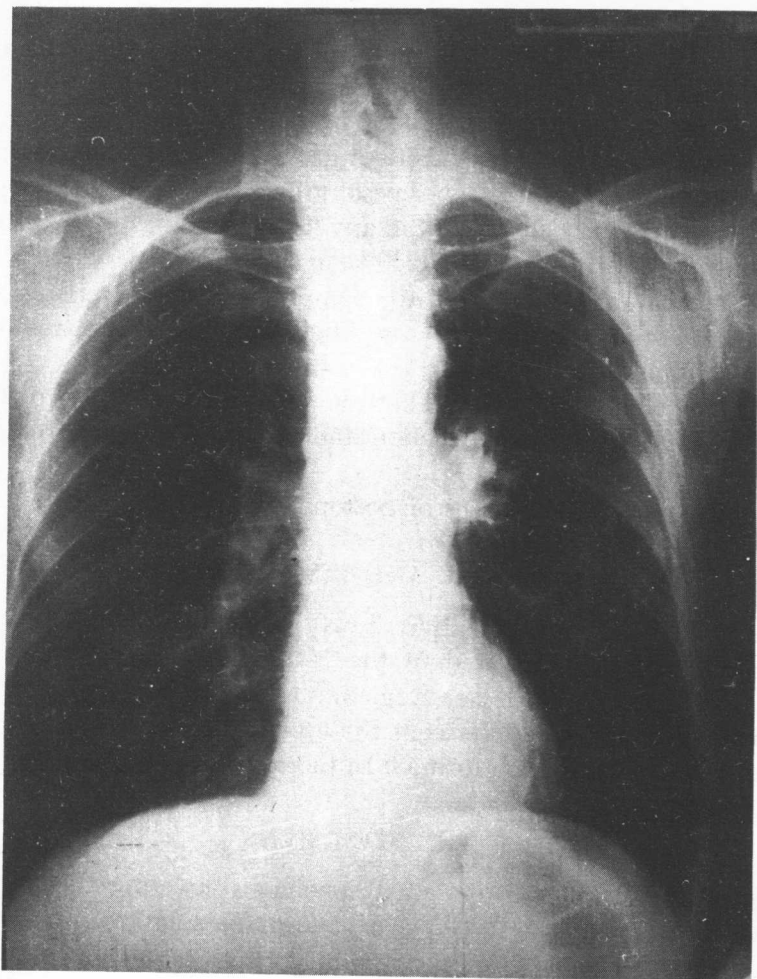
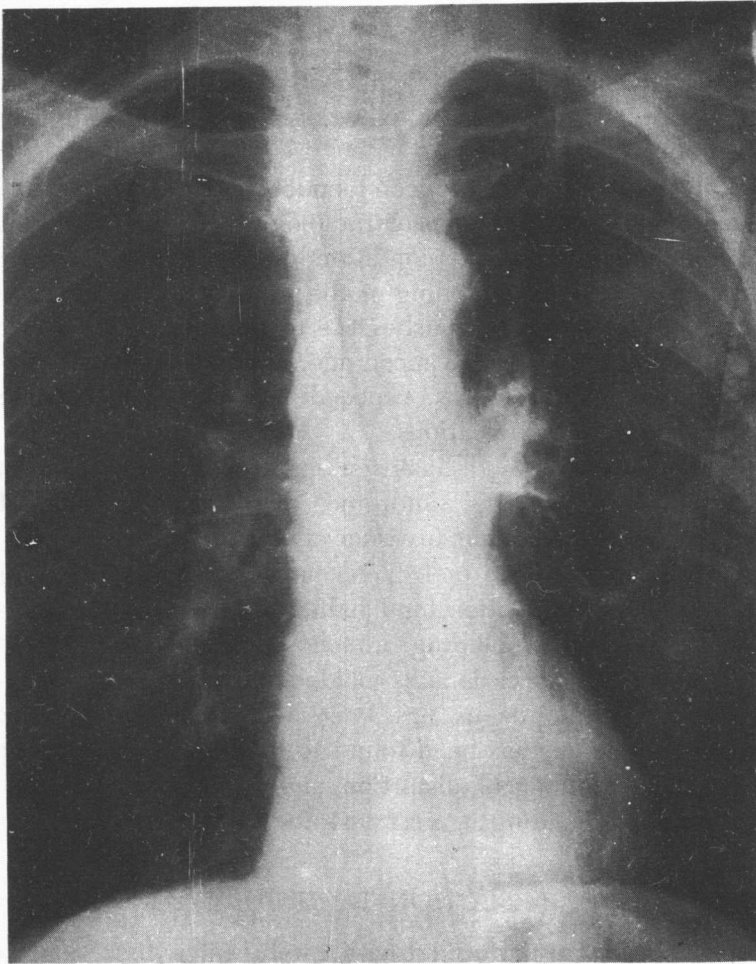


Fig. 4. Chinaman, aged 53. A. Film of 12/6/54. True diagnosis doubted by practitioner because of a positive Wassermann reaction.

From the specimens, some 992 lymph nodes—that is, an average of five lymph nodes per specimen—were dissected and examined histologically. This task was entrusted to Dr. E. K. Dawson and her staff, Dr. W. Lees and Dr. J. D. McGregor of the Pathology Research Laboratory of the Royal College of Physicians of Edinburgh.

At this stage I wish to pay tribute to the work of Dr. Dawson and her colleagues. They painstakingly examined and reported on each one of the sections with all the care and insight that was the tradition of that Edinburgh group of histopathologists trained under the late Colonel Harvey.



B

Fig. 4. B. Film of 9/23/55. Nine months of delayed diagnosis. Left upper lobectomy, 10/19/55. Epidermoid carcinoma of lung. Nine years later (10/19/64), still fit and well.

This work can well be criticized in that, because three representative sections were at most made through each lymph node, a relatively large volume of each node was left unsectioned. Since it is not at present economically possible to section, let alone examine, every cell layer in even one lymph node, however, the research is presented as it was carried out and must be judged in that light. Similar difficulties and criticisms are equally applicable to related studies on carcinoma behavior in other organs, such as the rectum, breast, and stomach.

INDICATIONS FOR RESECTION

Mason (6) has stated the indications for resection used in the North Regional Thoracic Surgical Centre, Newcastle-upon-Tyne, England, at the time of this study.

✓ Exploratory thoracotomy is recommended in all cases without obvious contraindications, such as clinical or radiologic evidence of dissemination of growth, inadequate general condition of the patient, bronchoscopic evidence of distortion and widening of the bifurcation of the trachea, and extension of the growth dangerously close to the bifurcation of trachea or into the mediastinal viscera. Advanced age, poor cardiorespiratory reserve, emphysema, and arteriosclerosis, especially coronary insufficiency, have been shown to be contraindications.

Although as yet no growth has been operable in the presence of recurrent nerve palsy or Horner's syndrome, diaphragmatic palsy does not conclusively indicate malignant invasion of the phrenic nerve, which may be injured by pressure alone or by associated inflammation. Empyema is certainly *not* a contraindication, and habitual and complete investigation of all cases of empyema, including bronchoscopy and bronchography during convalescence, has occasionally yielded an operable growth. Barium examination of the esophagus has long been standard practice, for a patient whose esophagus has been found to be grossly distorted has rarely proved operable. Esophageal distortion alone, however, has never been the sole reason for deciding against operation.

RESECTION TECHNIQUE

All operations were performed with careful hilar dissection technique. All surrounding lymph nodes were removed, as was the pericardium if it had been invaded.

MEDIASTINAL DISSECTION AT OPERATION

Total mediastinal block dissection of all soft tissue, including lymph nodes, was carried out in some resections, especially during 1950.

On the right side this involved removal of the entire mediastinal pleura and the right side of the pericardium, including the areolar tissues and lymph nodes. Such dissection laid bare the trachea, superior vena cava, and esophagus with its associated right phrenic and vagus nerves.