

LUNG  
CANCER

SEYMOUR M. FARBER, M.D.

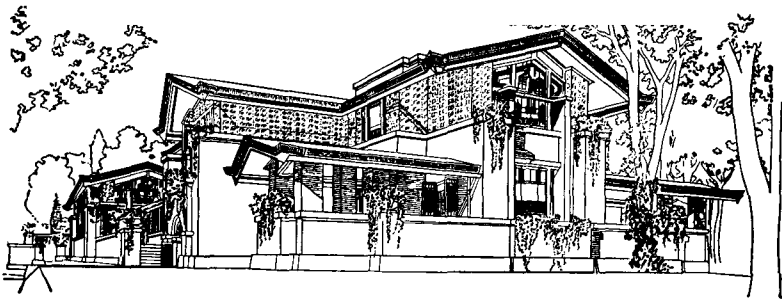


# **Lung Cancer**

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# Introduction

*By*

J. ARTHUR MYERS

THE RECENT phenomenal increase in knowledge of prevalence, diagnosis and treatment of cancer of the lungs has made imperative the preparation of a concise and practical volume containing all available facts concerning this disease. His long, intensive study of pulmonary malignancy, his extensive clinical experience, his investigative spirit, and his vision of the solution of the problem have admirably qualified Seymour Farber for the preparation of such a volume.

This monograph is the result of 10 years of constant study and observation in the field of bronchogenic carcinoma. Such a period is almost nothing in the observation of persons with a lifetime disease like tuberculosis, but with cancer, which moves with such swiftness and usually kills with such promptness, a decade of observation is adequate to justify conclusions.

The procedures here recommended and the conclusions drawn were based upon 1,070 autopsies which were carefully studied both clinically and pathologically. These necropsies were performed in 19 California hospitals of all types, each employing a registered pathologist. This insured broad and basic material. In addition, 3,000 persons suspected of having lung cancer were admitted for cytological studies of sputum and bronchial secretions, along with other differential diagnostic procedures, in the laboratory of the University of California Hospital.

One of the most important sources of material was the author's private practice, which provided an opportunity to study general practitioners' problems and viewpoints, as well as unique experiences in diagnosis and treatment of cancer. He first presents a broad pattern of etiology, histopathology, roentgenology, diagnostic aids and treatment for all cancer and then focuses on that of the lung.

This book is rightly directed to those in general practice, who compose the overwhelming majority of physicians throughout the world. It is they who most often have the opportunity to make the first examination of the individual who is developing cancer. Therefore, general practitioners are and must continue to be in the front line in the fight against this disease. In order to hold that line they must be adequately equipped with the latest techniques in diagnosis and treatment, as well as the best general information available. General practitioners, in turn, are the ideal group to transmit information concerning cancer to the public. This they do personally through the families of their clients, and through cancer control organizations. Without full cooperation of the public, further progress in the control of this condition will be slow.

With a relatively long, silent period in its early evolution and with its host usually becoming aware of the presence of illness only after metastases have occurred, people everywhere should learn that cancer must be found before there are manifestations of illness if its victims are to be treated successfully.

The most serious handicap in the entire control movement is lack of a specific test to indicate the presence of the disease while the lesions are still microscopic, such as we now have in the tuberculin test for tuberculosis. Learning through such a test that cancer is present somewhere in a given individual's body, the physician

could make oft repeated examinations of those parts most frequented by this disease and locate the lesions as soon as they attain sufficient size to be detected. Thus one might expect to locate and remove most cancers before they have metastasized. While awaiting such a test for cancer, much can be done to improve the present situation.

Although he recognizes that the only successful treatment of cancer today is surgical extirpation, the author, like many other workers in this field, has a deep conviction that the future treatment of pulmonary cancer will be with drugs. Therefore he has outlined this complex field in such a way as to make all physicians more sensitive to developments in chemotherapy in the future.

It is heartening to see emphasis placed upon the responsibility of physicians caring for persons who have inoperable or recurrent carcinomas. At present, this constitutes at least 90 per cent of all who have cancer of the lungs. It has been estimated that there are some 30,000 inoperable cases of bronchogenic carcinoma just in the United States. The author says, "A real challenge to the physician's art is a patient who is inoperable at diagnosis or has post-operative recurrence." He then proceeds to present step by step the physician's armamentarium in coping with this situation.

Dr. Farber's extensive and long experience in the front line of the fight against cancer of the lungs, along with his constant teaching of formal medical school courses, lecturing before medical societies, presenting postgraduate courses for both specialists and physicians in general practice, and personal conversation with many practicing physicians have enabled him to grasp the needs of all physicians. He has met these needs simply, concisely, and yet so completely that it is a privilege to speed this volume on its way to physicians everywhere.

## Acknowledgments

**B**ECAUSE successful treatment of bronchogenic carcinoma is radical, and because of the complexity of the subject generally, it is sometimes assumed that the disease is a problem for specialists. It is, of course, a problem concerning many kinds of specialists, but it is also a clinical problem of great magnitude, the immediate concern of all engaging in the practice of medicine. The typical patient with lung cancer does not present himself at a cancer clinic, or a university hospital when symptoms first become apparent; he comes to medical attention routinely. This book has been written from the point of view, then, of the clinician, upon whose judgment other members of the medical profession must depend.

It is impossible to acknowledge all the obligations that are represented in a book of this kind. Every professional man with whom I have discussed the subject in the last 10 years has, in one way or another, contributed to this study. But there are special contributions which cannot be neglected. Drs. Mortimer A. Benioff, E. Fred Alston, Milton Rosenthal, James G. Tobias, Allen K. McGrath, Jr., Lloyd W. Espen, Walter H. Buel, Judith D. Smith, Jesselene H. Thomas, and Richard F. Barquist are, or have been, my colleagues in this study. They constitute the group without which this book could not have been written. Dr. Cameron Ward has generously given of his time in reading the manuscript. William Brandt, of the University of California English Department, has been assiduous in his numerous and valuable suggestions

for shaping the prose style toward maximum clarity and conciseness, and Miss Eleanor Little has checked the entire manuscript for conformity with established medical usage. The aid of Dr. Irving Reingold in securing photomicrographs is gratefully acknowledged. Lastly, I should like to express my gratitude for the devotion displayed by my secretaries, Sadie Kaye and Jean Mulcahy. Mistakes of one kind or another there must be in a book, but the co-operation I have received has been of immense help in reducing such errors.

S.M.F.



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# **Lung Cancer**



## **Etiology** | **1**

THE MODERN physician is of necessity a practical man. If he has the inclination to master the complex theory characteristic of the advanced fields of medical research, he has not, generally, the time. His professional life is primarily concerned with people, not theory, and whatever view the scientist puts forward, the physician's interest in disease remains a therapeutic one, an interest in man's afflictions. His questions are always specific. With each patient, his first question must be, "What affliction?" and his second, "What can be done about it?" The theory underlying a particular diagnosis and remedy is of secondary concern.

But all virtue to excess is vice, and the practicality of the physician can become impractical. A disease is not, after all, a collection of signs and symptoms responding uniformly to specific procedures. A disease is an abnormal process, a dynamic process, brought about by exterior interference with normal function, or by a specific physiologic disturbance. It has a cause, or coordinate causes. To approach disease from any less comprehensive point of view is to risk serious error. There are, of course, certain diseases, such as lobar pneumonia, in which a well-marked, "classic" appearance can be anticipated with some confidence. In such instances diagnosis can, with some safety, be a more or less routine evaluation of signs

and symptoms. Few of the major diseases of the thoracic cage, however, are so regular in their progress that such a routine approach to diagnosis is possible. Disease is conflict, and the symptoms and appearances that result are seldom specific enough to add up regularly and mechanically to the correct answer. Consequently, the serious afflictions to which man is subject are very likely to be approached by a system of trial and error, a process of elimination which the patient does not always survive.

The record of the medical profession in the diagnosis of bronchogenic carcinoma is regarded as unsatisfactory. Our own findings are in conformity with published studies. We have surveyed 1,070 cases of bronchogenic carcinoma, morphologically proven, collected from 19 hospitals in California.\* In 61 per cent of these cases, no positive diagnosis was made prior to autopsy. Compared year by year, it apparently took as long to make a correct diagnosis of the disease in 1949 as it had in 1935 (Figure 7).

Most of this difficulty arises from the absence of any kind of "classic" case of bronchogenic carcinoma, its most common characteristic being its protean manifestations. Thus, there is no available model form of the disease to serve as an accurate measure for diagnosis of the individual instance. Surely in these 1,070 cases the possibility of bronchogenic carcinoma frequently occurred to the examining physician soon after the patient required medical attention, only to be rejected as unlikely on the basis

\* The co-operation and help of the pathologists and staff of the following hospitals is gratefully acknowledged: Birmingham V.A. Hospital; Cedars of Lebanon Hospital; Fairmont Hospital; French Hospital; Highland-Alameda County Hospital; Los Angeles County Hospital; Letterman General Hospital; Marine Hospital; Mt. Zion Hospital; Oakland V.A. Hospital; Permanente Hospital; San Francisco City and County Hospital; San Joaquin County Hospital; Santa Clara County Hospital; Stanford University Hospital; St. Luke's Hospital; University of California Hospital and Wadsworth V.A. Hospital.

of inadequate signs and symptoms. As a consequence, diagnosis of the disease too often depended upon a protracted course of evaluation by elimination or other diagnostic possibilities.

Barring an innovation in diagnostic technique, any substantial improvement in the current diagnostic record requires a sounder approach to the disease. Diagnosis requires an understanding of the disease process which underlies and gives rise to clinical appearances rather than a check list of signs and symptoms. Such a basic approach can produce a much higher percentage of early diagnoses than are now obtained. This approach requires some knowledge of, and interest in, the actual course of a disease, beyond that which is visible to the eye and measurable by diagnostic techniques.

The research worker's interest is centered in etiology and pathology for improvement of techniques for controlling the disease; the practicing physician must concern himself with the same subjects primarily for their service to diagnosis.

The problem of bronchogenic carcinoma, however, cannot be isolated from the problems of malignancy in general, and the whole subject is dependent upon our knowledge of normal physiologic behavior. As has been pointed out many times, the problem of cancer is ultimately a problem in tissue growth, and the difficulties which arise when a coherent and comprehensive theory of cancer etiology is attempted reflect the complexity of normal cell development.

Although there are still large gaps in our knowledge of the latter subject, the general outlines of the process seem to be clear enough. Most important to an understanding of malignancy is the well established fact that a normal fissionable cell (with which cancer research is especially concerned), does not have a single principle of



development and control. Its course is governed by two distinct control mechanisms. Basically, such a cell is limited in its potential development by its inherent structure which is determined ultimately by an enzyme or enzymes. An undifferentiated cell may mature into one of several mature cell types, but the range is limited. As an instance, the undifferentiated, basal cells of the bronchi may develop into ciliated epithelial cells, non-ciliated epithelial cells or goblet cells. In the presence of a mechanical or infectious irritation, such cells may approach squamous stratified epithelium. But this completes the range of normal possibilities. Every undifferentiated cell, according to the "territory" in which it arises, has a similar selection of mature forms into which it may develop. Such a development is irreversible, and a mature cell cannot itself divide.

Upon these individual cells, already limited by their enzyme structure, the requirements of the whole organism are imposed. The operation of this secondary control seems at times to be mechanical, but more important to such control is the complicated system of hormones and related substances which direct and integrate all bodily processes. By this means the mature form that a particular cell will assume is determined. Likewise, the needs of the organism as a whole determines the rate of production of undifferentiated cells, by fission, and the rate of maturation. Both in clinical work and experiments with animals, it has proven virtually impossible to detect the precise nature of this hormonal activity. It is an open question whether an administered hormone operates by direct operation in all instances or by the suppression of other and native substances. However, there is reason to believe that the behavior of undifferentiated cells is generally determined by the total balance which is main-