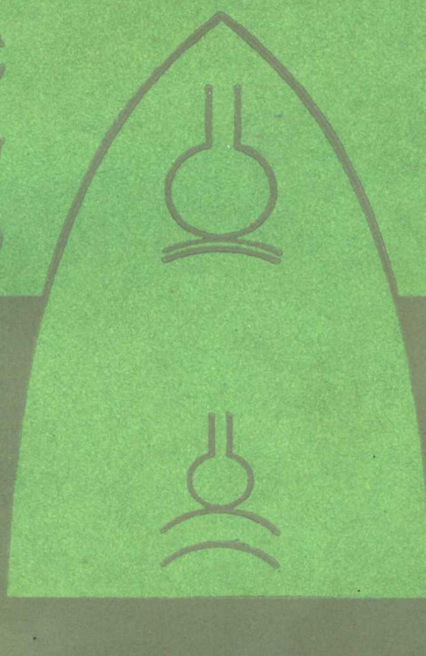
Regional Differences in the Lung



Edited by

John B. West, M.D., Ph.D.

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PREFACE

The chief aim of this book is to collate the results of research of the past fifteen years on the causes and consequences of regional differences of function and morphology in the lung by various groups of workers. This is an area of knowledge that received little attention until the 1960's, but in which very rapid and extensive advances have now been made. Many of the reports are scattered throughout a number of journals, and this volume aims to provide an up-to-date and comprehensive discussion of the entire field.

To achieve an understanding of the physiological mechanisms determining topographical differences within the lung is the central theme of this work. Since these mechanisms have many important consequences in a number of areas of medicine, the practical applications of the new knowledge are also emphasized. For example, regional differences of pulmonary function are of great significance in the causes of postoperative hypoxemia, the detection of early disease of the airways, the localization of pulmonary tuberculosis and emphysema, pulmonary edema complicating heart disease, interpretation of lung scans, and in the limits of man's tolerance to high acceleration. Moreover, physiological studies have far outstripped their application in these related fields. Thus, this volume should be of interest not only to physiologists, chest physicians, and cardiologists, but also to those working in the fields of anesthesia, nuclear medicine, and aerospace medicine.

In spite of the magnitude of the topographical differences of function in the lung and their clear implications in many areas of medicine, it is remarkable that virtually all the definitive measurements have been made in the last two decades. Indeed, physiology textbooks published as little as five years ago frequently made no mention of the subject. It was the introduction of radioactive gas methods that resulted in very rapid advances, and the amount of expensive equipment required has to some extent limited the number of centers which have made contributions. Even today it could be argued that the complexity of modern counting and display techniques sometimes blurs the scientific questions which are being asked. At any

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event, the rapidity of progress in this new field has made it increasingly difficult for all but those most closely connected with it to remain thoroughly informed.

The first chapter is devoted to a historical survey of early research on regional differences in the lung, and, in particular, to the large amount of work which has been done by sampling with catheters inside the bronchial tree. The next chapter deals with the principles of radioactive gas methods which have proved to be so fruitful in this area. The succeeding chapters then deal, in turn, with the various aspects of pulmonary function which show topographical variation, including blood flow, ventilation, gas exchange, pleural pressure, stresses, and edema. Finally, there are chapters on the exaggeration of these differences by acceleration, active mechanisms that may modify the regional differences, and the measurement of closing volume, one of the newer aspects of this field that has applications in clinical medicine and epidemiology.

Naturally some of the chapters are less definitive than others. For example, while the mechanisms of uneven blood flow and ventilation in the lung (Chapters 3 and 4) are now reasonably well understood, some of the material on transpulmonary pressures (Chapter 6) is controversial; research on the distribution of stresses (Chapter 7) is in its infancy, and data on the distribution of pulmonary edema (Chapter 9) are meager indeed. However, each chapter reflects the current state of knowledge and each has an extensive bibliography. Perhaps the obvious inadequacies of our understanding in some areas will stimulate further research.

I am indebted to the contributors who are acknowledged authorities in their disciplines, to Dr. Philip Hugh-Jones and Mr. John Clark for their helpful comments on Chapters 1 and 2, and to Mary Ann Bennett for her secretarial assistance. It is a pleasure to thank the staff of Academic Press for their help.

My contributions were written while I was a Josiah Macy, Jr., Foundation Faculty Scholar.

John B. West

CONTENTS

1

NONRADIOACTIVE METHODS

John B. West

1.1 INTRODUCTION

Of all the organs in the body, the lung is the most vulnerable to gravity and acceleration. There are several reasons for this. One is that the blood in the pulmonary capillaries is separated from the air in the alveoli by an extremely thin membrane over a vertical height of some 30 cm. As a consequence of the much greater density of blood compared with air, substantial pressure differences across the capillary walls therefore exist at different levels in the lung, and these result in marked topographical differences of blood flow and blood volume. Another reason is a combination of the weight of the lung and chest wall and the lung's great distensibility. The result is distortion of the lung tissue with consequent regional differences in ventilation, lung expansion, and mechanical stresses.

Most of the work on defining the distributions of blood flow and ventilation in the lung has been carried out by means of radioactive gas techniques.

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These methods were introduced in the 1950's and are discussed in detail in Chapter 2. Before these methods became available, however, a good deal of information on topographical differences within the lung had been obtained by sampling within the lung with catheters. The first measurements of this type date back to the last century, but recent advances using a respiratory mass spectrometer combined with the modern flexible bronchoscope have resulted in a resurgence of interest in this area. In addition, some information on regional differences in the lung has been obtained by radiographic techniques, and also by the analysis of expired gas under certain conditions. This first chapter is devoted to these nonradioactive methods.

1.2 SAMPLING WITHIN THE LUNG

1.2.1 Introduction

The earliest method of obtaining information about the function of a region of the lungs consisted of inserting a tube into the bronchial tree. In an extensive review, Björkman (1934) states that the first attempt was made in 1871 by Wolffberg using a catheter with two concentric tubes (Fig. 1.1).

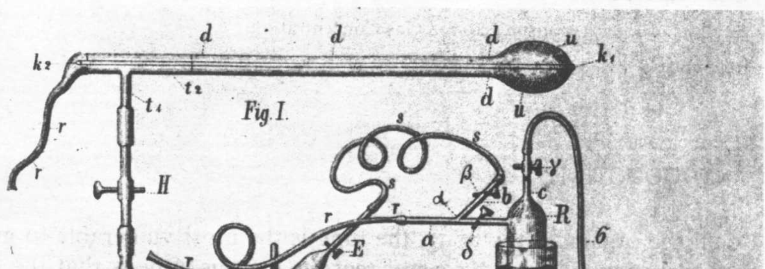

FIG. 1.1 Catheter and associated equipment used by Wolffberg (1871) who was apparently the first to sample gas from a region of the lung. The top portion of the figure (*Fig. I*) shows the catheter itself with the inflatable balloon marked *u*. The lower portion (*Fig. II*) shows the equipment for collecting alveolar gas from the catheter. (From Wolffberg, 1871.)

The outer tube had a thin wall at the distal end so that it could be inflated to occlude a bronchus; gas could then be aspirated from the lungs through the inner tube. In his "Leçons sur les anesthetiques et l'asphyxie" of 1875, Claude Bernard described the results of allowing one lung of an animal to breathe carbon dioxide and the other air. However, no details of the technique were given. Head in 1889 made measurements on a tracheotomized rabbit by passing a cuffed tube (inflated with glycerine) into one main bronchus and another tube into the trachea.

The experiments reported by Maar in 1904 are of interest. He tied cannulas into each bronchus of rabbits, and showed that partial compression of the left pulmonary artery reduced the oxygen consumption and carbon dioxide excretion of that lung. These changes were often accompanied by increased gas exchange in the other lung, and were not affected by injections of atropine or section of the vagi.

Loewy and Schrötter (1905) have the distinction of being the first to attempt measurements of regional lung function in man. They used a modified Pflüger catheter (Fig. 1.2) but were concerned only with blood gas measurements

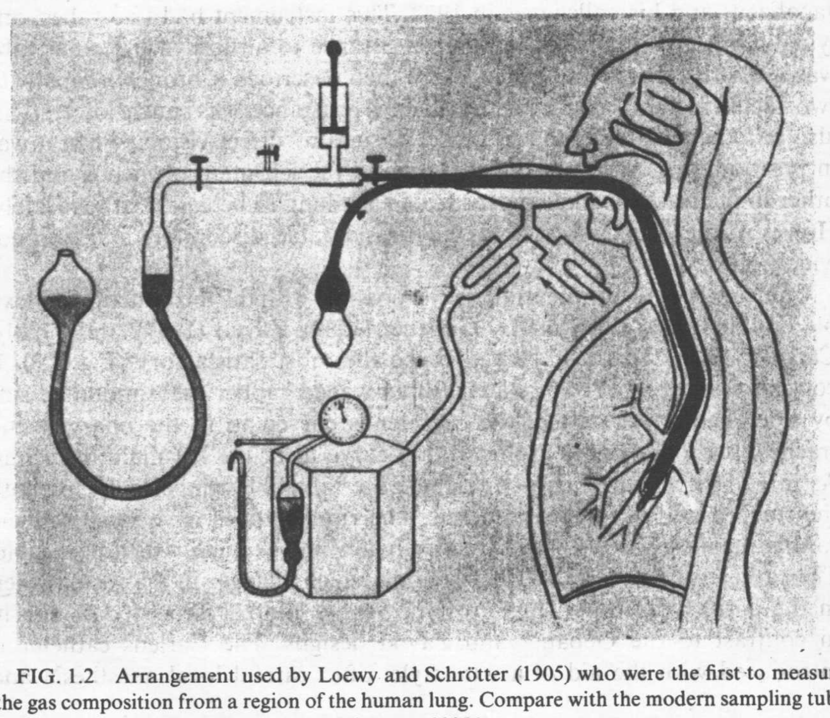

FIG. 1.2 Arrangement used by Loewy and Schrötter (1905) who were the first to measure the gas composition from a region of the human lung. Compare with the modern sampling tube shown in Fig. 1.4. (From Loewy and Schrötter, 1905.)

and did not study ventilation. An important advance was made by Mathieu and Hermann in 1925 when they introduced the double-lumen catheter. This was thin walled with a central septum so that each tube had a D section. At the distal end, the two tubes separated to lie in each main bronchus, and a notch was provided to fit the carina. Each tube was connected to a spirometer, and these workers measured the ventilation of each lung in tracheotomized dogs, and related this to the lung volumes measured after death.

In 1926, Churchill and Agassiz reported some interesting experiments in which they studied the separate effects of compressing the left pulmonary artery, pulmonary veins, and main bronchus on the ventilation of each lung in cats. They used separate spirometers for the two lungs, and found that obstruction of the left pulmonary vein apparently increased the ventilation on that side.

1.2.2 Bronchospirometry

1.2.2.1 *Description*

Valid simultaneous comparisons of the function of one lung with the other began with the introduction of the double-lumen bronchoscope by Jacobaeus and his colleagues in 1932. This instrument had two tubes, one lying within the other, but the high resistance to airflow of the outer tube was a disadvantage. Frenckner (1934) then described a bronchoscope with two identical tubes in which the airflow resistance was much lower. This also had the advantage that it could be sited by direct vision. When it was in position, two cuffs were inflated, one in the left main bronchus and the other in the trachea, allowing gas from each lung to be collected separately. However, the bronchoscope caused considerable discomfort and was not widely used.

Clinical bronchospirometry became possible with the introduction of flexible double-lumen catheters by Gebauer (1939), Zavod (1941), and, finally, Carlens (1949). This last proved to be the most satisfactory (Fig. 1.3). It consists essentially of two relatively thin-walled rubber tubes mounted side by side. The upper part of the catheter is curved to fit the pharynx and trachea, and one tube is extended in a curve to fit the left main bronchus. As in Frenckner's bronchoscope, there are inflatable rubber cuffs for both the trachea and left main bronchus. The rubber tubes have large calibers so that the airflow resistance is relatively low and exercise tests are possible. The catheter is fitted with a rubber hook which engages in the carina when in the correct position. Thus no fluoroscopic control is needed to site it, in contrast to the Gebauer and Zavod designs. The Carlens catheter is introduced with the aid of a wire stylet after careful local anesthesia and

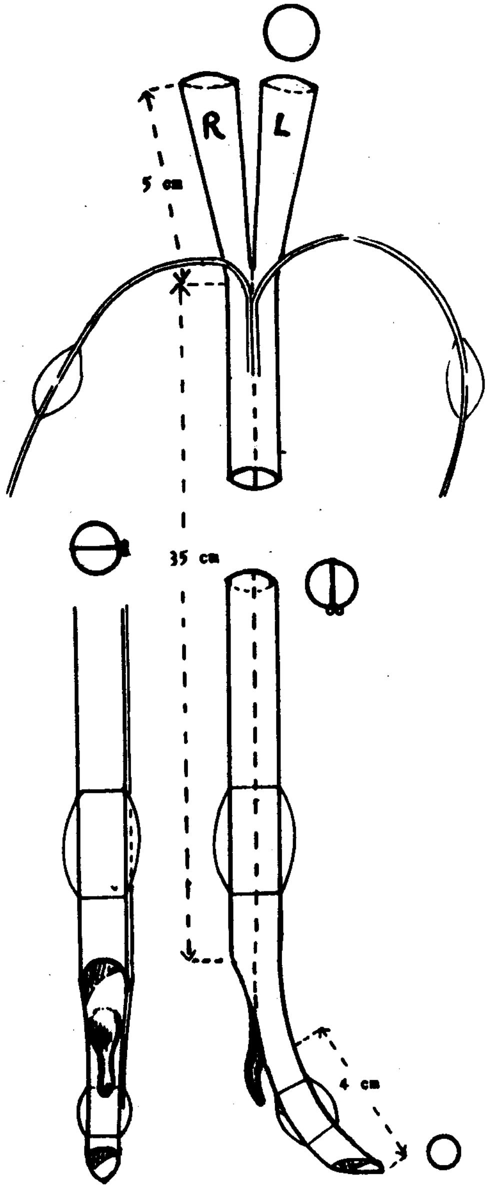

FIG. 1.3 Bronchospirometry catheter introduced by Carlens. It consists of two thin-walled rubber tubes. One of these extends into the left main bronchus and is provided with an inflatable cuff. Note the rubber hook which engages on the carina. (From Carlens, 1949.)

premedication. In practice, bronchospirometry by a trained team causes little more discomfort to the patient than bronchoscopy and many patients claim to prefer it to a visit to the dentist (Fleming and West, 1954).

1.2.2.2 *Information Gained by Bronchospirometry*

Normally, each tube of the double-lumen catheter is connected to a closed circuit containing a spirometer filled with oxygen. Two pens thus record the minute volume and oxygen uptake of each lung. Because of the high oxygen mixture, the oxygen consumption is virtually independent of the ventilation-perfusion ratio or the diffusing capacity for oxygen of the lung and is proportional to the pulmonary blood flow. If a closer approximation to the normal oxygen uptake of each lung is desired, the spirometer may be filled with air and oxygen trickled in at a measured rate as it is consumed.

Many physiological data have been collected by bronchospirometry. Measurements in normal volunteers have shown that about 55% of the total minute volume and oxygen uptake (breathing a high oxygen mixture) are accounted for by the right lung (Björkman, 1934). Several investigators have measured the function of one lung with the subject in the right and left lateral positions and found that both the minute volume and oxygen uptake are increased when the lung is in the dependent position (Björkman, 1934; Vaccarezza *et al.*, 1943). Measurements of oxygen uptake have been made under a variety of conditions. Carlens, Hanson, and Nordenström (1951) in man and Dotter and Lukas (1951) in dogs showed that unilateral occlusion of the pulmonary artery arrested the oxygen consumption on the affected side. Björkman and Carlens (1951) recorded the oxygen uptake on exercise in patients with pulmonary disease and concluded that the increase in oxygen consumption of each lung was proportional to the consumption at rest. Rahn and Bahnson (1953) in dogs and Himmelstein, Harris, Fritts, and Cournand (1958) in man demonstrated a reduced perfusion in a lung which was made hypoxic by lowering the inspired oxygen concentration. Studies of experimental atelectasis have been made by aspirating gas following a forced expiration. Björk and Salen (1950) induced atelectasis in dogs and showed that some perfusion of the atelectatic lung persisted for many hours. Bence and Lanari (1942) studied unilateral atelectasis in human volunteers.

A great many investigations by bronchospirometry have been made in a variety of diseases. Gaensler *et al.* (1953), for example, were able to analyze the results of 1000 examinations. The procedure has proved its worth in clinical investigation particularly in the assessment of patients for thoracic surgery, and it can give information hitherto unattainable by any other technique.

1.2.2.3 *Limitations of Bronchospirometry*

A serious objection to bronchospirometry is the relatively unphysiological state under which the measurements are made. An important feature of all three double-lumen catheters is the high resistance they offer to airflow. Gaensler, Maloney, and Björk (1952) have compared this with the resistance of the normal human bronchial tree. While the pressure difference between alveolus and mouth for a tracheal flow rate of 60 liters per minute is normally about 1.6 cm of water (Otis *et al.*, 1950), the pressure drop across a Carlens catheter carrying the same flow is about 4 cm of water. This increased resistance to airflow will adversely affect the performance of the lung in several ways. For example, the respiratory frequency is usually reduced and hypoventilation may even occur. The resting respiratory level (FRC) is generally increased by 200 to 1500 ml (Gaensler, 1952).

A further objection is that it is only possible to compare the left lung with the right using the technique described. This means that although the investigation is frequently valuable, it is a very insensitive tool for measuring regional lung function since abnormal behavior of a segment or lobe may be overshadowed by the rest of the lung on that side. This drawback was overcome in part by the introduction of a triple-lumen catheter.

1.2.3 Measurements with Triple-Lumen Catheters

In 1955, Mattson and Carlens described a special bronchospirometric catheter which allowed them to separate the gas going to the right upper lobe from that going to the rest of the right lung. They studied seven patients who had minimal pulmonary tuberculosis in the left lung, and were able to show a relatively low oxygen uptake in the right upper lobe which increased considerably when the subject lay supine (the spirometers were filled with oxygen). This increase in blood flow was accompanied by a small mean increase in ventilation which, however, was not statistically significant.

These findings were largely confirmed by Martin and Young (1957), who carried out similar measurements in nine subjects who had normal lungs or minimal tuberculosis on the left. They showed that the right upper lobe took up a mean of 38% of the total oxygen on the right when the subject was supine, but only 22% when he was erect, and that this reduction in blood flow was accompanied by a small but statistically insignificant decrease in ventilation. These authors were able to argue from their data that there must be a difference between the carbon dioxide tensions of mean alveolar gas and arterial blood because of these inequalities of the ventilation-perfusion ratio.

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