

Lung Biology in Health and Disease

Volume 2

Executive Editor: Claude Lenfant

The Biochemical Basis of Pulmonary Function

edited by

Ronald G. Crystal

THE BIOCHEMICAL BASIS OF PULMONARY FUNCTION

Edited by

Ronald G. Crystal

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FOREWORD

Many techniques for updating and assimilating new information in medicine have been proposed. As scientific reports proliferate, we hear shrill complaints about the amount of material that must be covered by the scientist and the physician in order to "keep up" with the latest and best information. There is no substitute for review by an expert to help others interpret the significance of new data and concepts.

This series of monographs is both expert and timely. There has been an expansion of research on respiratory and pulmonary problems. This expansion reflects a renewed public awareness of the importance of lung disease and a new awareness by researchers of opportunity to apply modern biological techniques to the study of the lung in health and disease.

It is my view that this series makes a comprehensive contribution to the science and practice of medicine and to the hopes we have for more effective concepts of preventive medicine.

Theodore Cooper, M. D.
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and Welfare

PREFACE

Our understanding of the mechanisms underlying the function of any organ is limited to our ability to devise "monitors" of that function. For the lung, that function is the exchange of gases between the blood and the atmosphere.

Early monitors of lung function utilized morphologic methods, such as chest films and light microscopy, to define normal lung structure and its alteration with disease. The limits of these monitors in understanding lung function led to the development of a sophisticated physiologic technology which yielded remarkable insights into how blood and air are brought into intimate contact in the alveolus to provide efficient gas exchange. Concurrently, morphologic monitors became quantitated, so that morphologic-physiologic correlates of lung function are now available.

It is the primary thesis of this volume that these morphologic-physiologic relationships are maintained and controlled by complex biochemical mechanisms from within and outside the lung. It is our purpose to describe in detail what is known about these biochemical mechanisms, thus adding "biochemical monitors" to the methods by which the mechanisms of lung function are understood.

Each of the first four sections of this volume deal with a major part of the biochemical basis of pulmonary function. In Part I, "The Cells of the Lung," the chapters by Kuhn and Gould detail the cell types in lung, the sub-cellular organelles which define biochemical function and the techniques necessary to disperse the lung into individual viable cells that can be studied with biochemical methods. Part II, "Basic Metabolic Functions of Lung," includes chapters by Fisher, Tierney, Levy, Mason and Collins which describe the mechanisms of energy production, carbohydrate metabolism, lipid metabolism and protein synthesis used by lung cells to maintain normal lung structure and function. In Part III, "The Connective Tissue of Lung," Hance, Horwitz, Elson and Cohen define the connective tissue composition of lung and describe how these components are maintained by intra- and extra- lung mechanisms. Part IV, "The Surfactant System of Lung," includes detailed descriptions by Clements, King, D. Massaro and G. Massaro of the biochemical basis of the maintenance of lung structure and function by the composition, synthesis, storage and secretion of the surface active lining layer of the alveolus.

In Part V, "The Interrelationships of Lung Biochemistry, Structure and Function," we have attempted to provide a composite view of the cellular and extra-cellular composition and organization of lung and correlate this information with the currently defined mechanisms by which lung structure and function is maintained. For the most part, we have dealt with the lung as an adult structure which has one purpose: gas exchange. We have not approached the mechanisms of how the lung differentiates in fetal life nor do we discuss the role of the lung in maintaining the endocrine environment of the body. We have also ignored most of the mechanisms involved in defending the lung against environmental insults. These topics are discussed in detail in other volumes in this series.

It may be premature to use the title "The Biochemical Basis of Pulmonary Function" as we are far from completely understanding all of the mechanisms controlling lung function. We hope, however, that this volume will provide the groundwork for what will become the major area of interest for investigators of pulmonary function. As we learn more about the mechanisms underlying the maintenance of lung function, we are closing the gap between our present technology and the time when we will be able to control these mechanisms in human lung disease.

Ronald G. Crystal
Bethesda, Maryland

ACKNOWLEDGMENTS

In the Spring of 1971, Donald Fredrickson, then Director of the National Heart and Lung Institute Intramural Division (now Director of The National Institutes of Health), developed the concept that the Pulmonary Branch of the NHLI should utilize multidisciplinary approach to the study of lung structure and function with major emphasis on the biochemical basis of lung function. Since this program started in July 1972, he has been a constant source of encouragement, advice and support for which I am grateful.

The problems dealt with in pulmonary biochemistry are far too complex for a single individual to thoroughly encompass. A greatly satisfying aspect of developing the Pulmonary Branch of the National Health Lung Institute has been my association with the creative individuals who are its members. They constantly devote their energies to understanding the biochemical basis of pulmonary function, and one-third of this volume is their work. I thank Katherine Bradley, Sally McConnell-Breul, James Collins, Norton Elson, Morton Cowan, Allan Hance, Allen Horwitz, Jack Fulmer, William Wagner, Charles Berkovich, Lillie Mack, Edwyna von Gal, Joanne Curtis, Kirsten Cook and Nancy Wyne for their intellectual stimulation, devotion to an ideal and very hard work.

For more than twenty years, John Clements has continued to probe at the complexities of the surface lining layer of the lung. His work is a model of how an organ as complex as lung can be dissected biochemically in order to define physiologic phenomena. The concepts he developed have led to the understanding, for the first time, of the biochemical basis of a lung disorder.

The contributors to this volume share our enthusiasm for this field, and their work speaks for itself. I am grateful for their cooperation and suggestions.

The 1972 NHLI report on pulmonary research and training programs categorized biochemical research as a very small fraction of lung research. Claude Lenfant, the editor of the series of which this volume is a part, has, through his position in guiding NIH funding of lung research, played the major role in greatly expanding the emphasis now placed on biochemical approaches in lung research in this country. In doing so, he has irrevocably altered the

direction of pulmonary research so that it now stands as a model for other fields of biochemical science.

My first publication was a letter in the New York Times in 1955 in response to an article on the complexities of the English language. Diana Winters, who helped edit this volume, is constantly reminding me of my continued ignorance of this subject, and for that and her detailed efforts, I am grateful.

INTRODUCTION

This volume, *The Biochemical Basis of Pulmonary Function*, is the second of the series in "Lung Biology in Health and Disease." As the Executive Editor of this series of monographs, it gives me great pride to introduce this volume. Indeed, Dr. Crystal has conceived a unique book which encompasses many aspects of lung biochemistry never published together before.

It is only during the last decades that pulmonary research has clearly included the investigation of the nonrespiratory functions of the lung. First in this line of investigation was work on the composition, synthesis, and degradation of the surfactant. Undoubtedly, this work—actively pursued in the United States and abroad—led to major discoveries of fundamental importance and of great clinical significance. However, only the "top of the iceberg" was examined. Today, the biochemistry of lung connective tissue, the capability of the lung to synthesize lipids and proteins, and the metabolism of lung tissue are intensively studied, together with studies on the morphology and function of the many types of cells comprising lung tissue. Clearly, it is only by looking collectively at all these facets that the complexities of the biochemical bases of lung function can be appreciated, if not yet fully understood. This monograph achieves the goal of bringing together the ideas and work of many investigators who have pioneered in the field. It is a tribute to Dr. Crystal to have so successfully edited this book, which, it is hoped, will stimulate the creativity of many other investigators.

Claude Lenfant, M.D.
Bethesda, Maryland

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Part I

THE CELLS OF THE LUNG

