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MICROBIOLOGY THIRD EDITION

MICROBIOLOGY

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Cover illustration: Recombination between two DNA molecules, visualized at the stage where a strand of each has been opened and its ends have been connected with those of the other opened strand. (H. Potter and D. Dressler, Proc. Natl. Acad. Sci. USA 74:4168, 1976) For further details see Figure 11-11.

MICROBIOLOGY

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To the memory of W. Barry Wood, Jr. (1910-1971),

who assembled the group of authors for the first edition of this text. His perspective and judgment as a coauthor contributed a great deal to its style, and his spirit still pervades the present volume.

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PREFACE TO THE THIRD EDITION

This textbook continues to be designed for the student who seeks to understand microbiology and immunology in some depth, and as a growing science. Hence despite the pressures for space we continue to try to indicate the nature of the evidence underlying each major conclusion, rather than only summarizing existing knowledge.

To make room for the new material nearly every paragraph has been rewritten. In addition, we have eliminated some detail in areas that are also covered in biochemistry courses (energy production, biosynthesis, and protein synthesis). However, we have expanded another biochemical topic, metabolic regulation, because it integrates molecular genetics with metabolism and with microbial ecology, and because studies in bacteria and in bacteriophages are continuing to provide profound new insights. Moreover, we have retained the chapters that provide a background in molecular genetics, since advances in bacterial physiology and virology, and now also in immunology, depend heavily on the concepts and the technics of this subject.

The most dramatic recent advances have been the discovery of several mechanisms for rearranging nucleic acid sequences (both in nature and in the laboratory), and the development of simple technics for isolating and sequencing short segments of DNA. This material will appear in many places—in the chapters on Organization of the Genetic Material, on Animal Cell Cultures, and on Multiplication of Animal Viruses; in a new chapter on Plasmids and Gene Manipulation; and in a reorganized chapter called Immunoglobulin Molecules and Genes. Cellular and molecular aspects of immunology have also advanced explosively, requiring a new chapter on the Cellular Basis of the Immune Response, and major revision of most of the chapters in immunology. A third area of rapid growth has been the molecular analysis of cell surfaces, including the attachment sites of bacteria and of host cells, and the various cell receptors involved in immune responses. Indeed, from these studies, and from molecular studies on bacterial toxins, complement, and inflammation, a true molecular biology of bacterial infections is emerging.

Authorship of the various sections and chapters is noted in appropriate places. In the section on virology, Dulbecco was responsible for general virology and the tumor viruses, and Ginsberg for multiplication of animal viruses, viral pathogenesis and the specific agents. Overall editing for uniformity of style was provided, except for certain chapters on specific viruses, by Davis.

Since immunology and virology are now often taught in separate courses, the sections on these subjects will also be made available as separate volumes.

The late W. Barry Wood, Jr. initiated this text, and his contributions are still present throughout the section on Bacterial and Mycotic Infections. He would have been pleased to see how his often expressed vision of a molecular biology of infectious diseases is now being realized.

> B. D. Davis R. Dulbecco H. N. Eisen H. S. Ginsberg

PREFACE TO THE FIRST EDITION

"What is new and significant must always be connected with old roots, the truly vital roots that are chosen with great care from the ones that merely survive."

This principle, professed by the composer Bela Bartok, is as applicable to science as it is to music. Indeed, it highlights the most difficult aspect of writing a modern textbook of microbiology, for few branches of natural science have been so rapidly altered by recent advances. Only a few years ago microbiology was largely an applied field, concerned with controlling those microbes that affect man's health or his economic welfare, but with the recent development of molecular genetics, stemming largely from the study of microbial mutants, microbiology has rapidly been drawn to the center of the biological stage.

As a result, infectious disease no longer constitutes the sole bridge between microbiology and medicine. An additional, rapidly broadening span is provided by the use of microbes as model cells in the study of molecular genetics and cell physiology, for the principles and the successful approaches developed in such studies will surely prove widely applicable to human cells, which can now be cultured much like bacteria. In addition, studies at a molecular level are also rapidly providing a deeper insight into problems directly related to infectious disease, including the action of chemotherapeutic drugs, the structure of antibodies and cellular antigens, and the nature of viruses. Hence to prepare the student for the scientific medicine of his future it has seemed to us desirable to increase emphasis on the molecular and genetic aspects of microbiology. At the same time, the authors, having all had clinical experience, are vividly aware of the importance of providing a thorough understanding of host-parasite relationships and mechanisms of pathogenicity, even though many aspects cannot yet be explained in molecular terms.

In short, we have tried to identify the "truly vital roots" of classical bacteriology, immunology, and virology, and to engraft upon them the recent molecular advances. To keep the volume to a reasonable size we have eliminated much traditional information that did not seem to have either theoretical or practical importance for the student of medicine. Moreover, the clinical and epidemiological aspects of infectious diseases have been largely left for later courses in the medical curriculum, and we have provided only a small number of selected references, primarily for access to the original literature and not for documentation. In the hope of making the book more useful and versatile, we have included in smaller type a good deal of material that seemed not essential for an introduction to the subject, but still likely to interest many readers.

The demands of the medical curriculum frequently lead to a condensed memorizing of conclusions; yet courses in the basic medical sciences should surely illustrate the scientific method as well as transmit a body of information. We have therefore briefly reviewed the history of many major discoveries in order to show how scientific advances may depend on new concepts or technics, or on ingenious experiments, or an alertness to the significance of unexpected observations. Moreover, we have endeav-

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ored throughout to indicate the nature of the evidence underlying the conclusions presented—for otherwise the student sees only the shadow and not the substance of science.

This book is designed primarily as a text for students and investigators of medicine and the allied professions: hence the exposition proceeds from general principles to specific pathogenic microorganisms. However, we hope that the discussion of general principles will also prove useful to graduate students and investigators in the biological sciences.

The preparation of this volume has been a truly cooperative effort: the chapters drafted by each author have been critically reviewed by most or all of the others. We are deeply grateful for the education and for the warm friendships that have resulted.

A new book of this size will inevitably contain errors and weaknesses. We shall welcome corrections and suggestions for future editions.

B. D. Davis R. Dulbecco H. N. Eisen H. S. Ginsberg W. B. Wood, Jr.

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We are grateful to the contributors who revised various chapters or portions of chapters. These authors should not be held accountable for any defects in expression, since their contributions were extensively modified to fit the style of the rest of the book.

We are also deeply indebted to the many colleagues who have critically reviewed various chapters. These consultants are listed on the following page. Special thanks go to A. M. Pappenheimer, Jr. for his extensive contributions to Chapter 26, and to Thomas J. Yang for the monumental task of checking the entire book for errors.

It is a pleasure to acknowledge the skillful help, pleasant cooperation, and patience of the publisher's staff and of our several secretaries, during the three years of preparation of this revision. In addition, we are indebted to the Marine Biological Laboratory at Woods Hole, Massachusetts; to the many investigators who provided illustrations; and to the publishers who granted permission to reprint figures. Sources are acknowledged in the legends. Finally, we gratefully note the skill of Stephen Shaw in preparing the new illustrations and the careful preparation of the index, from the perspective of a student, by Jonathan H. Davis.

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