

THIRD EDITION

VOLUME II

Edited by

Elliott Middleton, Jr.

ALLERGY

Principles and Practice

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INTERNATIONAL EDITION

Volume **II**

Third Edition

ALLERGY

PRINCIPLES AND PRACTICE

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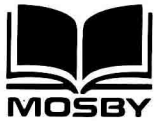
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To the clinical scientists who made this book possible,
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and to our basic science colleagues whose studies
paved the way to new clinical insights.

PREFACE to third edition

The second edition of *Allergy: Principles and Practice*, published in 1983, turned out to be a great success. This achievement was, of course, entirely attributable to the talents and efforts of the 119 contributors to the second edition. Now it is a pleasure to record that in this new third edition we have what we believe to be an exceptionally fine, truly “state of the art” addition to the literature.

The contents of the second edition represented some rather significant changes from the first as new information was rapidly accumulated in the field. Appreciating the perhaps even more rapid growth of new knowledge taking place in allergy and immunology during the past 5 years or so, of importance to clinicians and laboratory scientists alike, the editors and publisher concluded that a third edition would be desirable. To this end meetings were initiated toward the end of 1985. An important decision was made, however, before we went to work, namely, to add two new editors to the original group of three in order to enhance the quality and coverage of material in the third edition and to help ensure the longevity of *Allergy: Principles and Practice* as a primary textbook and reference source. The three original editors selected N. Franklin Adkinson, M.D., of Johns Hopkins University and John W. Yunginger, M.D., of the Mayo Clinic to join in the effort as co-editors. It will be clear to all that their contributions have enhanced every aspect of the third edition.

In keeping with editorial policy from the beginning, some changes in authorship for various chapters has occurred in the preparation of the third edition. In this fashion new and different talents and fresh points of view are brought to bear. The valuable work of contributors to the first and second editions is not lessened in any way by these changes and their splendid efforts in assuring the

success of the first two editions is acknowledged with great appreciation.

The third edition has 68 chapters contributed by 121 authors, 60 of whom are new to the book. Volume I continues as the source of basic information on the immunology, physiology, and pharmacologic aspects of allergic disease and Volume II remains the clinical science section; both are richly illustrated. Much new information has been included in Volume I reflecting the explosion of new fundamental understandings of the basic mechanisms involved in allergic disease, especially our knowledge of the nature, origins, and properties of proinflammatory chemical mediators that participate in the pathogenesis of allergic and inflammatory diseases and the biology of the cell types involved in allergic reactions. Volume II is thoroughly updated with regard to the essential clinical, diagnostic, and therapeutic aspects of allergic disease and should provide an authoritative source of information for practitioners in the specialty of Allergy and Immunology.

The editors gratefully acknowledge the time-consuming efforts of all contributors to the third edition, to their patient and tireless secretaries, and also to C.V. Mosby staff members Kathy Falk, Developmental Editor, and Ellen Baker Geisel, Assistant Editor, who did their best to keep us on schedule using their good humor and great organizational abilities.

As intended from the beginning, the third edition is an updated reference source as well as a thoroughly practical text. It is our hope that this book will be educational, and pleasing as well, to all who undertake its reading.

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Charles E. Reed
Elliot F. Ellis
N. Franklin Adkinson, Jr.
John W. Yunginger

PREFACE

to first edition

Allergy, once a confusing subject for clinician and researcher alike, has emerged as a medical science in which immunology, physiology, and pharmacology interface uniquely. Our present state of knowledge is the culmination of the efforts of many workers over many decades of research in the clinic and laboratory. We want to acknowledge our incalculable debt to these investigators, both basic scientists and clinicians, who taught us not only fact but more importantly concepts and scientific method.

Several textbooks on allergy are already in existence. Why another one? We pondered this question for some time before embarking on what turned out to be, expectedly, a rather formidable task. It was our opinion that a truly comprehensive book about allergy should focus strongly not only on the exciting developments of the past decade or two in immunology but also provide in-depth coverage of equally pertinent new information on physiology and pharmacology, two areas of critical importance to the student of allergy. We have made no attempt to cover all of the subject matter considered to fall under the general rubric of clinical immunology and so do not include sections dealing with rheumatology, other connective tissue disorders, immunohematology, or tumor immunology, for example, since these subjects are well covered elsewhere.

The chapters dealing with immunology, pharmacology, and physiology appear at the beginning in the basic science section of the book to provide the necessary conceptual framework for the clinical science section, which deals with the variety of clinical states that fall within the purview of allergy and the allergist. The value of the clinical descriptions is vastly enhanced by a careful reading of the earlier chapters.

We were most fortunate in securing a truly outstanding "star-studded" cast of contributors who managed to find time in their already overcrowded schedules to help us write the book. We thank them all for their efforts and are grateful for the patient indulgence of a few who put up with some predictable editorial fussing meant to achieve proper balance and avoid excessive overlap.

Most of the chapters can be read as free-standing articles or monographs on that particular subject. This has led to a certain irreducible amount of duplication. By and large, there is consistency among chapters in which comparable material has been presented by different authors,

but the reader will find occasional areas of controversy, a natural state of affairs in a rapidly growing field.

It is our opinion that some chapters in this book represent the most comprehensive summaries of the subject matter to be found in print. Thus *Allergy: Principles and Practice* serves not only as a textbook but as a reference book. Indeed, this was our intent, but original estimates for the length of the book were necessarily revised upward as it became clear that much excellent material could not properly be left out. The final product then turns out to be a book we hope will be useful to all students of allergy: practitioners, clinical investigators, other researchers, allergy trainees, and medical students.

The generous and unstinting help of many people in addition to the contributors made this book possible. Without the competent and devoted secretarial assistance of Marci Dame, Evelyn Beimers, Bonnie Barcy, Carol Sperry, and Candace Anderson, the task could not have been accomplished. We thank our wives and families for their forbearance while we were sequestered away from home for day and night weekend sessions during the planning and editing phases. From the beginning their support has been essential to the successful completion of our job. A number of colleagues, too numerous to name, provide help in critical reading of manuscripts. To these and others who were helpful in a variety of ways, we offer thanks.

We are saddened that two contributors died during the preparation of the book. Jane Harnett is the senior author of the chapter dealing with aspirin idiosyncrasy. Dr. Harnett compiled much of the information for the chapter and worked on the manuscript under extremely difficult circumstances up to within only a few days of her untimely death. She is remembered fondly and with respect by all those with whom she worked. Robert P. Orange, one of the most brilliant and creative investigators of his generation, died suddenly during the preparation of the book. No one can guess what additional important discoveries Dr. Orange would have made had he not died so prematurely.

We would like to record here our personal sorrow at the loss of these fine physicians. We hope that their representation in this textbook will help keep memories of them alive.

Elliott Middleton, Jr.
Charles E. Reed
Elliot F. Ellis

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volume **II**

CLINICAL SCIENCE

CELL-MEDIATED IMMUNITY IN HEALTH AND DISEASE

Burton Zweiman
Arnold I. Levinson

Clinical evaluation of CMI

- Skin tests for preexisting delayed hypersensitivity
- Skin test for primary delayed hypersensitivity responses
- In vitro studies in evaluation of CMI

Role of CMI in health and disease

- Defense against infections
- Rejection of foreign tissues: allograft (homograft) rejection
- Reaction against contactants: contact hypersensitivity
- CMI in atopic disorders
- Reactions against autologous tissues: autoimmune diseases
- Demyelinating and neuromuscular diseases
- Gastrointestinal diseases
- Endocrine disorders

Clinical states affecting CMI

- Anergy: what is it?
- Effects of age, pregnancy, and nutrition
- Transient depression of CMI
- Prolonged depression of CMI

Modulation of CMI

Summary: conclusions and speculations

Cell-mediated immunity (CMI) is the group of immune reactions thought to be mediated by sensitized T lymphocytes. In the early days of immunologic research CMI was considered to be primarily if not entirely, the delayed-type hypersensitivity (DTH) reaction against microbial antigens during the course of certain experimental and clinical in-

fections. After extensive research in recent years, it is now appreciated that CMI is a highly complex immunologic phenomenon expressed not only in DTH but also a number of biologic events of potential clinical significance.

This chapter will concentrate on the several roles of CMI in human immunoreactivity. By use of experimental and clinical examples, we will indicate (1) how a harmonious, efficient response may develop and result in protection of the host; (2) how an exaggerated response may lead to tissue damage, either in the reaction against microbial invaders (DTH) or possibly against host tissue components (autoimmunity); and (3) how indolence imposed by extraneous forces such as some systemic diseases frustrates the expression of CMI (anergy).

The current concepts of underlying mechanisms in CMI are discussed in detail in Chapter 13 and will be summarized only briefly here, with particular relation to the rest of this chapter. Despite considerable investigation, it is still not well defined how a small number of sensitized lymphocytes mediate the expression of CMI. On the basis of in vitro studies, one might postulate that the interaction of antigen and sensitized lymphocytes can, under appropriate conditions, through lymphokine elaboration: (1) attract monocytes, granulocytes, or both and increase adherence and metabolic activity of monocytes/macrophages—macrophage activation can be manifested by increased content and release of lysosomal enzymes, altered adenylate cyclase activity, bacteriocidal activity against certain intracellular microorganisms, and nonspecific toxic effects; (2) cause proliferation of other lymphocytes that are not sensitized to the antigen; and (3) lead to a direct cytotoxic effect on tissue.