GOODMAN and GILMAN's

The Pharmacological Basis of Therapeutics

SEVENTH EDITION

EDITORS:

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In this textbook, reference to proprietary names of drugs is ordinarily made only in chapter sections dealing with preparations. Such names are given in SMALL-CAP TYPE, usually immediately following the official or nonproprietary titles. Proprietary names of drugs also appear in the Index.

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PREFACE TO THE SEVENTH EDITION

THE first edition of this textbook, published nearly 45 years ago, was written when basic pharmacology was not fully accepted as a meaningful or relevant biomedical discipline. The appearance of that book did much to change the picture. An eminent pharmacologist, commenting on the first edition many years after its publication, stated that it provided a renaissance or perhaps more properly the *naissance* of the teaching and practice of pharmacology. The second edition, published in the mid-1950s, reflected the immense impact of the post–World War II burgeoning of biomedical research. Subsequent editions have been written as multiauthored works—a reflection of the enormous change in the content, stature, and function of pharmacology; its role in the biomedical sciences; and its impact on the clinical sciences and rational therapeutics. The Preface to the First Edition is reprinted herein, because it clearly states the three primary objectives that have guided the writing of all subsequent editions. Adherence to these objectives has encouraged widespread and successful use of *Goodman and Gilman's The Pharmacological Basis of Therapeutics* by students and practitioners of medicine and other health professions, both in the United States and abroad.

Those familiar with previous editions of this textbook will immediately recognize the organization of the present volume, which remains largely intact from the sixth edition. Nevertheless, the revision of the text has been extensive. This is a reflection not only of the dozens of new therapeutic agents that have become available to the clinician during the past 5 years but also of tremendous advances in both basic pharmacology and the application of that knowledge to medical practice. It is increasingly necessary for the pharmacologist to be a complete biologist, versed in biochemistry, physiology, biophysics, cell biology, and molecular genetics. Technics developed by molecular biologists are now having a profound impact in pharmacology. Molecular cloning of DNA and biosynthesis of the encoded products permit large-scale production of agents such as human insulin and growth hormone. Of even greater significance, detailed information on the primary structure of important macromolecules has become available as a result. These proteins include receptors for acetylcholine and insulin, the voltage-sensitive sodium channel, the receptor for low-density lipoprotein, and many others. While this could not have been anticipated a decade ago, the next few years will see an explosion of such information. To follow will be the capability to predict the tertiary structure of such proteins and, ultimately, to design drugs to alter their functions selectively and predictably. Coupled with these advances have been similarly impressive strides in such areas as mechanisms of receptor function, transmembrane signaling events, regulation of second-messenger synthesis, and so forth. Discussion of such topics appears throughout the textbook. Increased knowledge of pharmacokinetics and its practical application have kept pace with advances in pharmacodynamics. One indication of this growth is the near doubling of the drugs for which detailed pharmacokinetic data are presented in Appendix II. These are just a few of the major trends that are emphasized in the seventh edition.

Most of the contributors to the sixth edition were able and anxious to participate in the current undertaking, and we are pleased with this loyalty. We also welcome several outstanding new authors. Two of us are delighted with the efforts of the two new editors of this volume, Theodore W. Rall and Ferid Murad.

In addition to paying tribute to our collaborators, we gratefully acknowledge the advice and help received from scores of individuals, too numerous to mention by name. However, special note is made of certain extraordinary efforts. Michele Ferguson reviewed all sections of the text on pharmaceutical preparations and dosage with skill and exceptional

diligence. Dr. Murray Smigel catalyzed the passage of untold megabytes of text past the guardians of several computers. Our editorial assistants—Wendy Deaner, Jane Rall, and Kathryn Gilman—spent literally thousands of hours in the performance of countless tasks, almost all with outstanding good humor. The importance of their efforts cannot be overstated. We also note the special relationship between this textbook and Joan Carolyn Zulch, Publisher and Editor-in-Chief, Medical/Nursing/Health Sciences Department, Macmillan Publishing Company. Miss Zulch has edited this textbook for six editions over a period of more than 30 years.

Finally, we would like to record some of our feelings about Alfred Gilman, who wrote the first two editions of this textbook in collaboration with Louis S. Goodman and who served as an editor until his death in 1984. He was a gentle and unpretentious man; a kind and thoughtful colleague, friend, father. Alfred Gilman's major contributions to biology and medicine have been chronicled in detail by others; they spanned supervision of the first clinical trial of nitrogen mustard to the global review of drug efficacy undertaken by the National Academy of Sciences/National Research Council. He was committed to the integration of basic science and clinical medicine, particularly as a teacher, author, and editor. On the occasion of his receipt of an honorary degree in 1979, Dartmouth University President John Kemeny stated: "Far more than an isolated exercise in pharmacology, your book has provided for generations of students and practitioners the essential, but difficult, bridge between the basic medical sciences and the practice of medicine. Indeed, it could be said that long before the concept of an integrated curriculum became a popular educational philosophy in medical schools, it was a reality in the form of your textbook." We reaffirm this principle and dedicate this volume to the memory of Alfred Gilman.

ALFRED GOODMAN GILMAN
LOUIS S. GOODMAN
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FERID MURAD

PREFACE TO THE FIRST EDITION

THREE objectives have guided the writing of this book—the correlation of pharmacology with related medical sciences, the reinterpretation of the actions and uses of drugs from the viewpoint of important advances in medicine, and the placing of emphasis on the applications of pharmacodynamics to therapeutics.

Although pharmacology is a basic medical science in its own right, it borrows freely from and contributes generously to the subject matter and technics of many medical disciplines, clinical as well as preclinical. Therefore, the correlation of strictly pharmacological information with medicine as a whole is essential for a proper presentation of pharmacology to students and physicians. Furthermore, the reinterpretation of the actions and uses of well-established therapeutic agents in the light of recent advances in the medical sciences is as important a function of a modern textbook of pharmacology as is the description of new drugs. In many instances these new interpretations necessitate radical departures from accepted but outworn concepts of the actions of drugs. Lastly, the emphasis throughout the book, as indicated in its title, has been clinical. This is mandatory because medical students must be taught pharmacology from the standpoint of the actions and uses of drugs in the prevention and treatment of disease. To the student, pharmacological data per se are valueless unless he is able to apply his information in the practice of medicine. This book has also been written for the practicing physician, to whom it offers an opportunity to keep abreast of recent advances in therapeutics and to acquire the basic principles necessary for the rational use of drugs in his daily practice.

The criteria for the selection of bibliographic references require comment. It is obviously unwise, if not impossible, to document every fact included in the text. Preference has therefore been given to articles of a review nature, to the literature on new drugs, and to original contributions in controversial fields. In most instances, only the more recent investigations have been cited. In order to encourage free use of the bibliography, references are chiefly to the available literature in the English language.

The authors are greatly indebted to their many colleagues at the Yale University School of Medicine for their generous help and criticism. In particular they are deeply grateful to Professor Henry Gray Barbour, whose constant encouragement and advice have been invaluable.

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New Haven, Connecticut
November 20, 1940

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