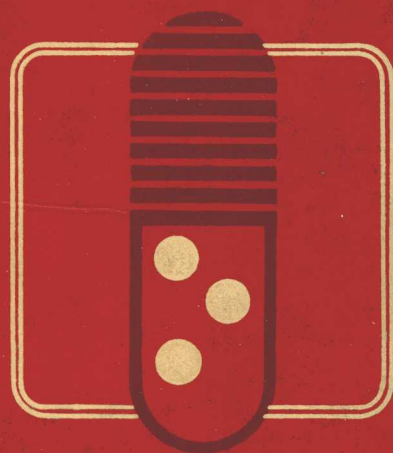
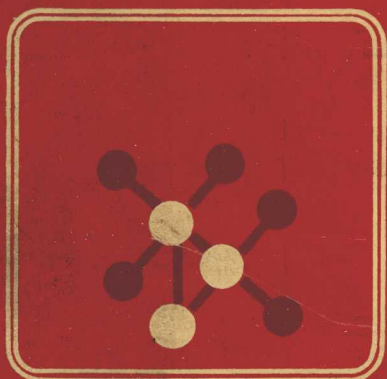


Essentials of

Pharmacology

THIRD EDITION



John A. Bevan
Jeremy H. Thompson

PHARMACOLOGY

Introduction to the Principles of Drug Action

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The authors and publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new or infrequently employed drug.

Third Edition

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PREFACE

After being frequently urged to write upon this subject, and as often declining to do it, from apprehension of my own inability, I am at length compelled to take up the pen, however unqualified I may still feel myself for the task.

The use of the Foxglove is getting abroad, and it is better the world should derive some instruction, however imperfect, from my experience, than that the lives of men should be hazarded by its unguarded exhibition, or that a medicine of so much efficacy should be condemned and rejected as dangerous and unmanageable.

(p. vi) It is now about ten years since I first began to use this medicine. Experience and cautious attention gradually taught me how to use it. For the last two years I have not had occasion to alter the modes of management; but I am still far from thinking them perfect.

It would have been an easy task to have given select cases, whose successful treatment would have spoken strongly in favour of the medicine, and perhaps been flattering to my own reputation. But Truth and Science would condemn the procedure. I have therefore mentioned every case in which I have prescribed the Foxglove, proper or improper, successful or otherwise. Such a conduct will lay me open to the censure of those who are disposed to censure, but it will meet the approbation of others, who are the best qualified to be judges.

To the Surgeons and Apothecaries, with whom I am connected in practice, both in this town and at a distance, I beg leave to make this public acknowledgment, for the assistance they so readily afforded me, in perfecting some of the cases, and in communicating the events of others.

The cases related from my own experience, are generally written in the shortest form I could contrive, in order to save time and labour. Some of them are given more in detail, when particular circumstances made such detail necessary; but the cases communicated by other practitioners, are given in their own words.

*An Account of the Foxglove, and Some of Its Medical Uses;
With Practical Remarks on Dropsy, and Other Diseases*
—WILLIAM WITHERING, M.D.

William Withering had a sufficient personal interest and knowledge of botany that he was able to conclude that the medical value of a local folk remedy containing many herbs lay in the foxglove. As a result of his personal observations on the use of this plant in dropsy (congestive heart failure), he learned what it would do and also its limitations. He was commendably slow to generalize and to commit himself in writing conclusions, nor did he try to hide his errors and failures—a most salutary attitude that no doubt was appreciated by his medical colleagues. Unfortunately modern medicine does not encourage such a leisurely practice and wide interests, but we hope that the principles are still followed whenever possible. They are reflected in the general philosophy of this textbook. It is often not the newest and the latest that are most important to master because many of these will be discarded before the student is responsible for his own practice. Rather, since drugs come and go, it is essential that the student-physician learn to ask the right questions and develop the right pattern of thought. A general understanding of pharmacologic principles and problems is the most important thing to be learned.

The dramatic increase in new remedies over the past decade, along with the complexity of the essential knowledge now necessary to use them wisely, has dictated a number of changes since our first two editions. Of greatest importance, the major contributor to the first two editions, Dr. Jeremy Thompson, has become a co-editor. His wide knowledge of medicine, therapeutics, and pharmacology as well as his experience in their intelligent communication is reflected in this new edition. We also welcome back many of our previous contributors and appreciate their suggestions, their support, and their enthusiasm. In addition a number of new and distinguished pharmacologists, physicians, and scientists are on our roster. Some have written completely new topics (*see below*), others have rewritten chapters that have appeared previously, including Prescription Writing; Central Nervous System Neurotransmitter Mechanisms and Psychopharmacology; Antidepressant Drugs; Antimanic Drugs; Neuroleptic Drugs; Sedative—Hypnotics and Antianxiety Agents; Drugs for Rheumatic Diseases; Opioids: Agonists, Antagonists, and Mixed Antagonist—Agonists; Cardiac Glycosides; Antiarrhythmic Drugs; Antihypertensive Drugs; Diuretics; Hormones of the Hypothalamus and Pituitary Gland; Pharmacology of the Thyroid Gland; Pharmacology of the Parathyroid Glands and Calcitonin; Insulin, Hypoglycemic Drugs, and Glucagon; Pharmacology of the Corticosteroids and Adrenocorticotrophic Hormone; Pharmacology of Androgens and Estrogens; Oral Contraceptives; Drugs Used to Treat Protozoal Diseases; The Vitamins; Commonly Used Intravenous Solutions and Diagnostic Agents; Prolonged-Action Dosage Forms; Therapeutic Drug Monitoring; and Sources of Information in Pharmacology. At the end of most chapters, a number of examination questions have been introduced. We are indebted to Dr. Sydney Ellis, author of *Pharmacology Review*—a comprehensive review for examination and self-assessment in the Arco medical review series—who has shouldered the responsibilities of this innovation. We hope that these questions will provide our readers the opportunity for self-assessment and lead to their better understanding of the textual material.

Scattered throughout the book are footnotes, small vignettes of historical and scientific interest prepared by Sandra Colville-Stewart, which we anticipate will bring life and flavor to these pages. To keep abreast of new developments, a number of new chapters have been added and others deleted. Specifically new chapters have been included on Principles of Drug-Receptor Interactions; Pharmacokinetics; Drugs That Affect

Uterine Contractility; Cyclic AMP as a Mediator of Drug Action; Prostaglandins; Pharmacology of Gastrointestinal Hormones; Vasoactive Peptides; Oral and Dental Pharmacology; and Parenteral Nutrition. Many of these topics were included in other chapters in previous editions but because of their recent emergence in importance have been designated as separate chapters in this 3rd edition. Because there is a more conservative approach to the approval of new drugs in the United States than in other countries, we have included a reference supplement prepared by Drs. Kevin O'Malley and Desmond Fitzgerald that covers those agents available for use in Europe but not in this country. Because some of these reference drugs may be approved for use in the United States during the lifetime of this edition, this material will be of use to those studying in this country.

Our sincerest thanks go to Nelly Canaan and Michelle Markel-Cohen for their untiring effort to bring together the scattered elements of this text. The patience and administrative skills required to accomplish this task can never be overestimated.

John A. Bevan, B.Sc., M.B., B.S.

PREFACE TO SECOND EDITION

For a perfect sight of the old medicine, let me conduct you to the bedside of Charles II: With a cry he fell. Dr. King, who, fortunately, happened to be present, bled him with a pocket knife. Fourteen physicians were quickly in attendance. They bled him more thoroughly; they scarified and cupped him; they shaved and blistered his head; they gave him an emetic, a clyster, and two pills. During the next eight days they "threw in" fifty-seven separate drugs; and towards the end, a cordial containing forty more. This availing nothing, they tried Goa stone, which was a calculus obtained from a species of Indian goat; and as a final remedy, the distillate of human skull.

Sir Andrew MacPhail
The Source of Modern Medicine, 1933

There is no doubt that the "new medicine" is different. Part of the progress is due to the adoption of a rational drug therapy based upon knowledge of the useful as well as the adverse effects of pharmacologic agents.

Many changes have been made in the second edition of this text. A number of new and distinguished authors have been added to the roster of contributors. The whole text has been revised, brought up to date and expanded, particularly into general pharmacology, the pharmacology of the peripheral and central nervous system and the endocrine glands, and anticancer agents. Completely new chapters have been added, including those on pharmacogenetics, drugs of abuse, poisons, alcohol, pediatric pharmacology and drugs used in the treatment of the hyperlipidemias. I would like to thank all those who made suggestions and gave advice on the reshaping of the contents.

As before, the text is designed primarily for medical and dental students although it would be of considerable value to those in the ancillary sciences of medicine, particularly pharmacy and optometry. Despite its modest increase in length it still remains a relatively short text, a distillate of essential pharmacologic knowledge, a sufficient core of knowledge upon which to base drug therapeutics of the new medicine. An understanding of its contents would be sufficient preparation for the National Boards in Pharmacology.

It is a pleasure to thank those to whom I am greatly indebted for their help in the preparation of this edition. The constructive critical review of various chapters by the following members of the Clinical Staff of the Center for Health Sciences, University of California, Los Angeles, is deeply appreciated: Victor D. Newcomer, M.D., Gary S. Rachelefsky, M.D., Ronald M. Reisner, M.D., Arthur D. Schwabe, M.D., Jerrold A. Turner, M.D., and Lowell S. Young, M.D. Dr. Jeremy H. Thompson has been a continual source of invaluable support, comment, and encouragement. Barbara Friedman has carefully drawn the new figures and helped remedy deficiencies in existing ones: Nell Crewe has assisted with typing. The staff of the Medical Department of Harper & Row have redesigned the layout of the text. Partial support for compiling the index was obtained from Roerig Division of Pfizer Pharmaceuticals. Finally, my sincere thanks go to Elizabeth Ainley without whose constant, meticulous help and management of the whole revisionary process this edition would not have been possible.

Los Angeles, California

J.A.B.

PREFACE TO FIRST EDITION

This textbook is based upon the course in pharmacology for medical and dental students given by the staff of the Department of Pharmacology, The Center for the Health Sciences, University of California at Los Angeles. These students have completed their preclinical studies and are commencing their clinical work. The aim is to present an essential core of pharmacologic knowledge sufficient for those proceeding to clinical clerkships, specific enough to guide others during internship, and yet provide a grounding in basic principles for both that will be valuable during the balance of professional life.

The text has been written within the constraints imposed by a recently adopted shorter curriculum. It has been recognized that although all students should understand the principles of the various basic sciences, and for professional reasons must assimilate and retain an essential compendium of facts, much that has been committed to memory in the past need not have been. Often detailed factual knowledge of a subject has been acquired at the sacrifice of a thorough understanding of its principles. Only the latter will prepare the student to understand and make new claims, developments, and advances. The authors of this book have attempted to effect a compromise between an understanding of the principles of drug action and the pragmatic requirements of practice.

Events of the past few years have drawn the attention of both professional and layman to the price we seem to have to pay for our increasingly bountiful therapeutic cornucopia. New drugs can control and cure disease and make our lives longer and more pleasant. Unfortunately, they cause undesirable adverse reactions, interfere with important laboratory testing procedures, and by their very number, often make the choice of the best drug in any particular instance difficult or impossible. For these reasons the adverse effects of drugs have been given unusual emphasis throughout the book. Until agents with new actions or safer substitutes for those commonly used are found, we must learn to use those we have more circumspectly.

Since this book is designed as a teaching text for students, it is not claimed to be a complete exposition of the discipline, nor to be an *infallible* guide to the clinical indications, uses, limitations, adverse effects, and dosage of drugs. The practicing physician is urged to check the drug package insert and other sources before administration especially if the drug is fairly new or used infrequently.

ESSENTIALS OF PHARMACOLOGY

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