ESSENTIALS OF
PHARMACOLOGY

OLDHAM • KELSEY • GEILING

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FRANCES K. OLDHAM, PH.D., M.D.
Associate Professor of Medicine
The University of South Dakota

AND

F. E. KELSEY, PH.D.
Professor and Chairman of the
Department of Physiology and Pharmacology
The University of South Dakota

AND

E. M. K. GEILING, PH.D., M.D.
Frank P. Hixon Distinguished Service Professor and
Chairman of the Department of Pharmacology
The University of Chicago

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Preface to the Third Edition

The third edition of this book retains the objective of the two preceding editions, namely, the presentation of a basic Pharmacology text in which the general principles of Pharmacology are stressed and the coming trends in the field indicated. As in the previous editions, the text is designed to give the student a broad and up-to-date survey of the present status of Pharmacology and to prepare him for evaluating future scientific advances.

The more extensive changes in this edition include the substitution of the chapter entitled "Miscellaneous Chemotherapeutic Agents" by two new chapters, one devoted to antitrypanosomal agents and the other to the chemotherapy of tuberculosis and leprosy. The chapter entitled "Arsenic and Bismuth Compounds" has been replaced by one entitled "Antireponemal Agents," a change dictated by the virtual abandonment of arsenicals in favor of penicillin in the treatment of syphilis. Other sections that have undergone extensive revision include those devoted to antimalarial drugs, to antihypertensive agents, to the endocrines and to the antibiotics.

Each chapter again concludes with a short bibliography and a list of important drugs compiled from the *Pharmacopeia of the United States* (fifteenth edition, 1955), from the *British Pharmacopoeia* (1953), from the *National Formulary* (tenth edition, 1955) and from *New and Nonofficial Remedies* (1955). Dosages, unless specified, are those of a single oral adult dose. Official, generic or chemical names are used wherever possible; proprietary names are indicated by capitalization of the initial letter.

The authors will be grateful for a continuation of the many helpful suggestions for improvement of subsequent editions.

THE AUTHORS

Preface to the First Edition

This book is intended to serve as an introductory text in Pharmacology. Much of the detailed documentary material necessary for the more advanced student or the research worker has been omitted, and scant mention has been made of such drugs as nicotine, strychnine and muscarine, which are of considerable importance from the viewpoint of pharmacodynamics but are little used in present-day medicine. On the other hand, the general principles of Pharmacology have been stressed wherever possible, and efforts have been made to indicate what appear to be the coming trends in the field.

The first course in Pharmacology in medical schools is usually given after preparation of the student in anatomy, bacteriology, biochemistry, physiology and pathology. Experimental pharmacology draws freely on all these sciences for its materials and methods, turning to the clinical sciences for help in those researches requiring the use of human subjects.

Pharmacology has also built a place for itself in other professional fields such as dentistry, nursing, pharmacy and veterinary medicine. Furthermore, popular knowledge of this science is becoming more and more widespread as the result of such dramatic advances as insulin, the "sulfa" drugs, penicillin and the new antimalarial agents.

At the end of each chapter, there is a list of important preparations of the drugs discussed and a fairly extensive bibliography. The preparations are compiled from the Pharmacopoeia of the United States, Thirteenth Revision, 1947; from the British Pharmacopoeia, 1932, including Addenda I-VII; and from New and Nonofficial Remedies, 1947. We have followed the U.S.P. XIII usages of English names for drugs and the metric system for dosage. For practical pur-

poses, the references have been largely limited to recent articles, written in English and published in readily available journals.

We are grateful to a number of colleagues who have read and offered criticisms of various chapters. In particular we are indebted to Dr. M. E. Davis of the Department of Obstetrics and Gynecology, to Dr. J. G. Allen, Dr. A. S. Alving, Dr. E. B. Bay, Dr. A. T. Kenyon, Dr. C. P. Miller, Dr. W. L. Palmer, Dr. H. T. Ricketts, Dr. S. Rothman and Dr. C. L. Spurr of the Department of Medicine and Dr. W. H. Taliaferro of the Department of Bacteriology and Parasitology of the University of Chicago; to Dr. J. J. Jacoby of the Department of Surgery of Ohio State University and Dr. F. F. Snyder of the Department of Obstetrics and Gynecology of Harvard Medical School. We are also indebted to our associates in the Department of Pharmacology, Dr. J. M. Coon, Dr. K. P. Dubois and Dr. J. R. do Valle, Guggenheim Fellow in Pharmacology and Professor of Pharmacology at São Paulo University, Brazil, for many constructive suggestions. We also wish to acknowledge the invaluable assistance of Mr. Wallace Tourtellotte, Research Assistant in Pharmacology.

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Historical Development of Pharmacology

Pharmacology is a compound word derived from the Greek terms *pharmakon* meaning medicine or drug and *logos*, a discourse or study. The science of pharmacology has been defined by Schmiedeberg as "an experimental science which has for its purpose the study of changes brought about in living organisms by chemically acting substances (with the exception of foods) whether used for therapeutic purposes or not."

Modern experimental pharmacology is one of our newest disciplines, as far as university organization is concerned, yet it had its beginnings in antiquity. Ever since man's advent on earth, one of his main concerns has been the alleviation of pain and suffering, consequently, each succeeding period of history has had its own system of healing based, in part at least, on the scientific concepts of the time. Early man sought a reason for pain and for disease processes; he ascribed them to the presence of evil spirits or considered them as punishments from the gods for wrongs he had done. The first remedies, accordingly, were intended to drive away the evil spirit or to punish the individual for wrongs done and were chosen for their disagreeable taste or odor.

In ancient times, as today, much suffering and disease ran their course or came to spontaneous remission regardless of the therapy used. Such recoveries gave an apparent validity to many remedies that were actually worthless.

On the other hand, some substances employed by fortuitous circumstances were of specific value in certain diseases and are part of our armamentarium today. Among the multitudinous recipes listed in Eber's papyrus, an Egyptian record of 1550 B.C., are such drugs as castor oil, colchicum and opium, which are still in use.

In the Egyptian period and even in the early Greek period, medicine was a part of religion and philosophy. The concept of disease as a pathologic process going on within the body, rather than as a visitation from the gods, was formulated for the first time by Hippocrates (460-370 B.C.) and marks the beginnings of scientific medicine. Accurate observation of the course of illness made it possible to classify and appraise the use of drugs. Unfortunately, the scientific principles of Hippocrates were not to be carried out fully until the dawn of the Renaissance many centuries later. With the decline of Greek culture, the quest for fresh knowledge was forgotten. Although medicine among the early Romans was an honored and important field, under the influence of Galen (A.D. 131-201) it degenerated into a dogmatic system of polypharmacy. Instead of furthering observation and analysis of actual processes, Galen sought the answer to medical problems in pure theory. Throughout the late Roman and medieval periods, Galen's theories were accepted and medical progress ceased.

With the Renaissance, however, the Hippocratic spirit was revived. Free thought and critical inquiry led Paracelsus (1493-1541) to attack the Galenic system of polypharmacy. He introduced simplicity in prescription writing and recommended the use of chemical substances rather than the mixed vegetable preparations of Galen. The treatment of syphilis with mercurials was inaugurated by Paracelsus. The first official pharmacopeia was printed in Florence in 1497.

The revolt against Galenic medicine, however, did not lead at once to the establishment of truly Hippocratic in-

quiry. By the seventeenth century, freedom of thought and individual scientific effort had led to a curious anomaly. While medical science was progressing, popular medicine was retrogressing. The same century that saw the use of the royal touch to cure the king's evil, and the exploitation of many useless remedies, also saw Harvey's epochal observation of the circulation of the blood and Malpighi's introduction of microscopic anatomy and the beginnings of animal experimentation.

These discoveries in the field of scientific medicine, together with the beginnings of modern chemistry and physics, formed the ferment out of which was to come modern experimental pharmacology. Throughout the eighteenth century men of science endeavored to classify and to correlate the new knowledge; it became the age of theories and systems. Théophile de Bordeu enunciated a theory of endocrine secretions, postulating that each organ serves as a factory for its specific humor, which is absorbed into the blood stream and carried to distant organs. William Withering introduced digitalis, after identifying it as the active ingredient in a recipe obtained from an old woman of Shropshire, thus establishing the rationale for another bit of successful folk medicine.

The organized advancement of modern pharmacology began with the nineteenth century. With the development of organic chemistry, isolation and identification of the active principles of crude drugs became possible, among the earliest being the isolation of morphine by Sertürner in 1804. Now for the first time, physiologic problems could be approached from the standpoint of chemistry and physics, an approach that marked the end of vitalism. Understanding of the transmission of infection and of the bacteriologic nature of many diseases opened new fields for therapeutics. The introduction of anesthesia led to great and rapid progress in the clinical and experimental fields.

Up to 1850, the French were leaders in scientific medical

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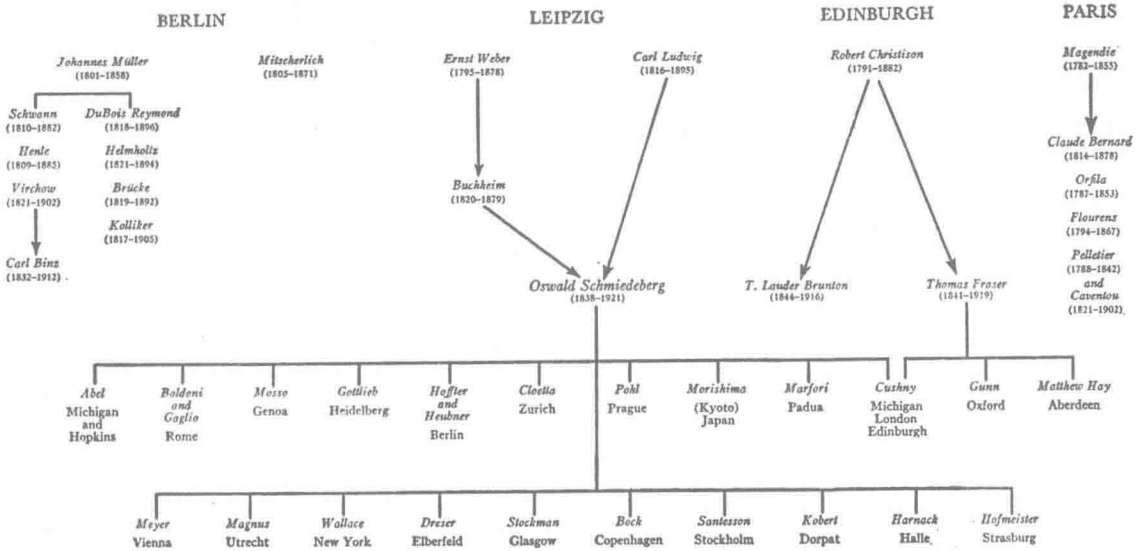

Forty Chairs of Pharmacology have been held by pupils of Oswald Schmiedeberg in many different countries. Those named above have been chosen to illustrate the international character of the school developed by him. A more complete list is given in his *Festschrift* volume of the Archiv. f. Path. u. Pharmakol., 1908, supplementary volume.