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Pharmacology and therapeutics

for dentistry

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Preface

Pharmacology and Therapeutics for Dentistry has been designed to meet a number of objectives which we believe are not adequately met in any single current textbook of pharmacology. The conviction that such a text is needed emerged out of our view, a view that is shared by many dental educators and professionals throughout the country, of what the dentist should know about pharmacology. It is a striking fact, which none of the basic medical pharmacology textbooks appears to recognize, that dentists write many prescriptions; it has been estimated that 65,000,000 prescriptions were written by self-employed dentists in the United States in 1975, and it is likely that this number will double by 1985. Moreover, dentists are prescribing an increasing variety of drugs to be used both in and out of their offices, and the dental patient is not uncommonly taking one or more medications which may have some impact on dental therapy or on drugs used in connection with such treatment. Finally, dentists are legally responsible for the total health of their patients while under their supervision and therefore must be thoroughly capable of discussing the entire spectrum of pharmacologic agents with medical and dental colleagues, hospital personnel, and the lay public.

With this pharmacologic profile of the dentist in mind, we have set out, with the invaluable help of our contributors, to write a book that would fulfill two major objectives: to provide the dentist with a thorough and basic understanding of the principles of drug action and of the specific pharmacology of all the major classes of drugs and, in recognition of the dentist's major concerns and problems, to provide deeper, more focused coverage of certain areas of pharmacology. These objectives are met in *Pharmacology and Therapeutics for Dentistry* in the following ways. First, every major class of drugs is covered thoroughly and with utmost contemporaneity. Second, certain sections (for instance, those on local anesthetics and antianxiety drugs) have been given somewhat fuller treatment than is provided in traditional medical pharmacology texts because the dentist makes very extensive and special use of these drugs. Third, several topics of unique interest to dentistry, such as anticaries-antiplaque agents and drugs used in pain and anxiety control, have been included. Finally, a number of chapters contain features that provide a uniquely dental focus for the book. For instance, the chapter on inflammation contains a full and up-to-date discussion of the mediators of inflammation and the pharmacologic agents that act on them; it also includes many important dental examples and applications. The chapter on antineoplastic drugs, while presenting a thorough discussion of the drugs used in cancer chemotherapy and their mechanisms of action, includes a section on the stomatotoxicity of antineoplastic drugs. In the chapters on antibiotics, the reader is told not only which are the drugs of choice for pneumonia caused by *Haemophilus influenzae* and

for gonorrhea but also which antibiotics would be appropriate for a periapical abscess, acute necrotizing ulcerative gingivitis, and acute suppurative pulpitis.

In every chapter where it is appropriate, sections have been included describing the dental use of the class of drugs, the special implications of these drugs for dentistry, and contraindications to their use. While we have not eliminated from consideration those classes of drugs not traditionally prescribed by the dentist, we have dispensed with the listing of dosages of all drugs except those that the dentist might prescribe or use clinically. Furthermore, in chapters on drugs that the dentist is not likely to use, we have limited the number of drugs mentioned to a few prototypes, since we want to stress the principles of pharmacology and not burden the reader with exhaustive lists of names. Most chapters contain a list of the drugs mentioned in the chapter and one or two proprietary forms of that drug. No attempt has been made to provide a complete list of all proprietary forms of a given drug; the trademarked representatives have been chosen randomly. We have also made a deliberate decision to eliminate or decrease coverage of certain areas that are amply explored in other basic science disciplines. For instance, vitamins and minerals are legitimately the province of biochemistry, and thus there is no chapter on these subjects. Endocrinology is traditionally taught in both biochemistry and physiology, so we have felt free to be rather selective about what to include under endocrine pharmacology.

In summary, we feel it fair to characterize *Pharmacology and Therapeutics for Dentistry* as a standard, basic, thorough textbook of pharmacology *and* therapeutics, written specifically with the needs of the dentist in mind. With this new book, the dentist should be able to understand basic pharmacology, to know how and when to use specific drugs and what dosage of these drugs to use, and to know how a patient's pharmacologic status will determine the treatment and medicine prescribed for that patient.

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Introduction

Pharmacology may be defined as the science of drugs, their preparation, uses, and effects. The term derives from *pharmakon,* the Greek word for drug or medicine, and *logia,* the Latin suffix traditionally used to designate a body of knowledge and its study. As an organized discipline, pharmacology is of recent origin, but the study of medicinal substances is as old as civilization itself.

HISTORY

Sir William Osler once said, "The desire to take medicine is perhaps the greatest feature which distinguishes man from animals." Although this argument has been vitiated by experiments involving self-medication in rats and other laboratory species, it nevertheless serves to illustrate the historic relationship between drugs and humankind. The use of natural products to cure disease and alter mentation dates back to the dawn of recorded time. By the writing of the Ebers papyrus (ca. 1550 B.C.), more than 700 prescriptions for various ailments were known. Many of the ingredients incorporated in these preparations—lizard's blood, virgin's hair, fly excreta—are humorous by modern standards, but also included were many compounds recognized today as pharmacologically active. A summary of folk remedies and other medicinals that have withstood scientific scrutiny would list such substances as opium (morphine), belladonna (atropine), squill and foxglove (digitalis), cinchona bark (quinine and quinidine), coca leaves (cocaine), and ma huang (ephedrine). The empirical study of plant derivatives and animal products must have been quite extensive to have been so fruitful.

A major hindrance to the effective use of these drugs, however, was the large number of materials usually present in apothecary formulations. For example, the most popular drug of the fifteenth century, triaca, contained over 100 separate components. Aureolus Paracelsus (1493-1541) was the first to recognize that the indiscriminate mixing of numerous substances did little but dilute whatever effective compounds may have been present initially. The focus of Paracelsus on single agents was refined by Felice Fontana (1720-1805), who deduced from his own experiments that each crude drug contains an "active principle" which, when administered, yields a characteristic effect on the body. One of the greatest scientific achievements of the nineteenth century was the isolation and objective evaluation of such active principles.

In 1803, a young German pharmacist, Frederick Sertürner (1780-1841), extracted the alkaloid morphine from opium. This singular achievement not only marked the beginning of pharmaceutical chemistry; it also led to a revolution in experimental biology. The availability of newly purified drugs and the standardization of existing biologic preparations encouraged pioneers like François Magendie (1783-1855) and Claude Bernard (1813-1878) to employ pharmacologic agents as probes in the study of physiologic processes. The use of curare by

Bernard for the elucidation of the neuromuscular junction is but one example of the successes obtained with this approach. Perhaps because drugs became associated with several biologic sciences and were of course considered under the domain of the various medical specialties, the development of pharmacology as a separate discipline was delayed.

Rudolf Buchheim (1820-1879) and Oswald Schmiedeberg (1838-1921) were the two individuals most responsible for establishing pharmacology as a science in its own right. Buchheim organized the first laboratory exclusively devoted to pharmacology and became the first professor of his discipline. A student of Buchheim's, Schmiedeberg founded the first scientific journal of pharmacology. More importantly, through his tutelage Schmiedeberg helped spread acceptance of pharmacology throughout the world. One protégé of Schmiedeberg was John Abel (1857-1938), generally regarded as the father of American pharmacology.

Once an obscure experimental science, the purview of pharmacology has expanded to such an extent that the subject has become an important area of study for all health professionals and holds certain interests for the lay public as well. In dentistry, the impact of pharmacology was formally recognized by the American Dental Association in 1934 with publication of the first edition of *Accepted Dental Remedies*.

SCOPE OF PHARMACOLOGY

Pharmacology is one of the few medical sciences that straddles the division between the basic and the clinical. The scope of pharmacology is so extensive that several subdivisions have come to be recognized. *Pharmacodynamics* is the study of the biologic activity that a drug has on a living system. It includes a study of the mechanisms of action of the drug and the exact processes that are affected by it. The influence of chemical structure on drug action (the structure-activity relationship) is also a concern of this branch of pharmacology. *Pharmacokinetics* deals with the magnitude and time course of drug effect, and it attempts to explain these aspects of drug action through a consideration of dosage and the absorption, distribution, and fate of chemicals in living systems. *Pharmacotherapeutics* is the proper selection of an agent whose biologic effect on a living organism is most appropriate to treat a particular disease state. It requires a consideration of, among many other things, dose, duration of therapy, and side effects of drug treatment. The practice of *pharmacy* involves the preparation and dispensing of medicines. Although pharmacists today are rarely called upon to actually prepare drug products, they can serve as a useful source of drug information for both the clinician and the patient. *Toxicology* is that aspect of pharmacology dealing with poisons, their actions, their detection, and the treatment of conditions produced by them. The importance of toxicology to modern life is continually underscored by new discoveries of chemical hazards in the environment. A final subdivision, *pharmacognosy,* is now a somewhat vestigial science. Essential at a time when most drugs were derived from plants, it literally means "drug recognition" and deals with the characteristics of plants and how to identify those with pharmacologic activity. Most drugs today are synthesized chemically, but phytochemistry, especially the synthesis of complex chemical structures by plants, remains of interest.

After a description of how the study of drugs is classified, it is appropriate to discuss what is meant by the word "drug." To the pharmacologist, a drug is any chemical agent which has an effect on the processes associated with life. This definition is obviously quite broad and ill-suited for many parties who define the term more restrictively to better serve their particular needs. The therapist, for example, considers as drugs those chemicals that are effective in treating disease states. To the lay public, drugs generally connote those substances that cause mental and psychologic alterations.

Finally, governmental agencies are concerned with the revenue derived from the taxes levied against the sale of certain substances or with public health problems associated with their use. Some of these agents, such as tobacco and alcohol, are legally sequestered, that is, by law they are considered "nondrugs." While pharmacologists have long recognized these agents as potent drugs, they are exempted from the usual governmental restraints and are not subject to normal scrutiny by the Food and Drug Administration. There are other substances which have gained such special status not by historical accident as did the above but by considerations of public health. Examples of these include chlorine and fluoride added to community water supplies and iodides mixed in with table salt. Lawsuits over the question of whether these public health measures constitute an illegal form of "mass medication" have been resolved by the courts, at least in part, through the categorization of these chemicals as legal nondrugs when they are employed in a specified manner for the public good.

Drugs to be covered in this text will include almost exclusively only those substances with a known therapeutic application. Even so, the potential number of agents for consideration is large—several thousand drugs marketed in a multiplicity of dosage forms and, in some instances, in a bewildering variety of combinations. To limit confusion, emphasis will be placed on single, prototypical agents which are representative of their respective drug classes. By this approach, an understanding of the properties of related agents can be more readily achieved; at the same time, differences which may exist between them can be highlighted. Finally, it is important to recognize that there are certain generalizations which apply to all drugs. These principles of drug action are the subject of the first four chapters of this text. A mastery of the concepts presented in these chapters is necessary for a thorough understanding of pharmacology, for the rational use of therapeutic agents, and for the objective evaluation of new drugs.

SECTION ONE

Principles of pharmacology