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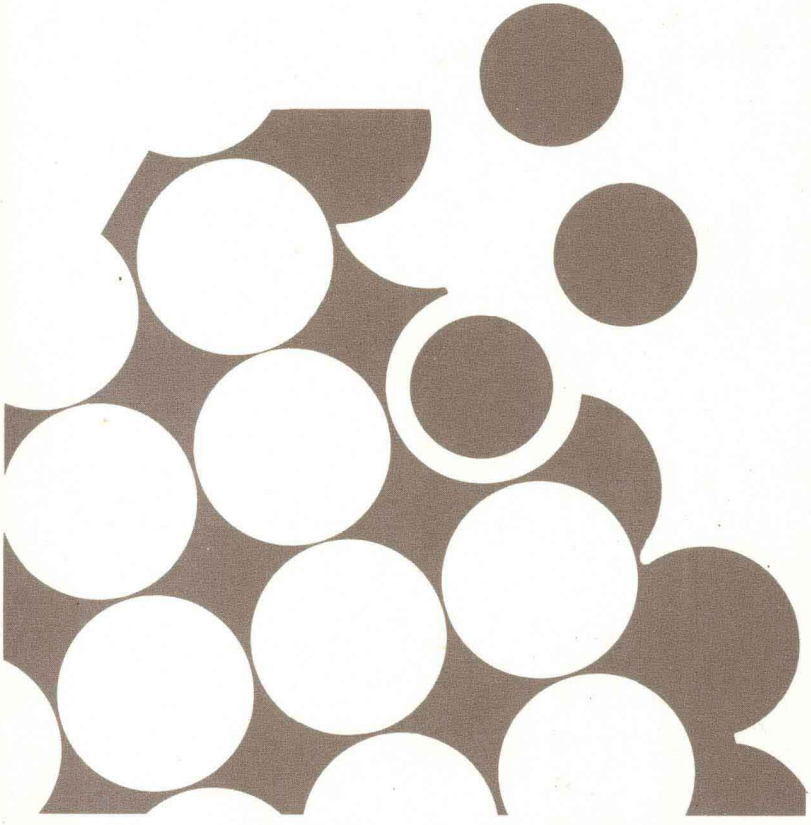

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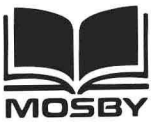

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This book is dedicated to the proposition that basic medical pharmacology is a living science that should be fun to learn, and that it should not be divorced from clinical medicine and clinical pharmacology.

DWN thanks his wife and family for their understanding and support, and Kenneth Melmon, M.D. for his wonderful introduction to the exciting blend of basic pharmacology and clinical medicine that is clinical pharmacology.

RPS thanks his wife and family and the generations of undergraduate, graduate, and medical students who collectively have taught him more than he has taught them.

PREFACE

Many of the major advances in modern medicine over the last 50 years have been in the improvement of diagnostic tests and medical therapies (e.g., modern drugs). Thus the basic medical pharmacology course, usually given in the second year of medical school, should be an exciting, relevant, and important course for all medical students.

However, many students feel that their courses are boring and irrelevant. They complain that there is an enormous amount of material to be memorized, and that this "dry" material does not seem to be relevant to their training as future physicians. Even worse, the facts memorized in the second year often seem to evaporate by the time the student begins to treat patients and encounter therapeutic problems during the third year.

We believe that introducing clinical problems during basic pharmacology courses will substantially benefit medical students—and dental, nursing, or pharmacy students as well. The problems for each chapter were written to stress several key concepts from that particular area of basic pharmacology. The 68 chapters in this book represent important areas of basic pharmacology that are common to most introductory medical pharmacology courses. Although certain pharmacology courses in specific schools may include more topics, we tried to cover those subjects that represent "core material" taught in the vast majority of courses.

The use of clinical problems (often adapted or condensed from real cases) not only demonstrates the clinical relevance of the basic science material, but also helps the student realize that problem-solving skills in pharmacology are as important as memorization of facts. In fact, patients present pharmacologic or therapeutic problems that must be solved; they do not demand a simple regurgitation of basic pharmacology facts.

Students in the second year of medical school are more sophisticated medically than is commonly believed by either students or faculty. They are quite familiar with common diseases such as cancer and hypertension; many have relatives who have had myocardial infarctions and strokes. Many have suffered the pain of a fractured bone, and some have undergone general anesthesia. In addition, many medical schools are beginning to introduce more clinical material into the first year of medical school, in the form of longitudinal outpatient clinics or clinical symposia. Thus, it is entirely appropriate to integrate elementary clinical material into basic science courses. In fact, it makes little sense not to do so!

We learn material best when learning is fun. As the student attempts to solve these problems, problem-solving and reference-searching skills will

be developed. By comparing his or her own answers to the model answers in the book, the student will discover where he or she erred in either the approach to the problem or the integration of the factual material. Whether these problems are attempted alone, in small informal groups, or in faculty-supervised seminars, they are designed to be fun.

If these problems are discussed in seminars directed by faculty, we hope they will present an opportunity for the students and faculty to work together and develop closer personal contact than can occur with the large lectures common in most medical schools during the first 2 years.

We firmly believe that a specific, separate course in clinical pharmacology should be given in every medical school during the fourth year. The exercises in this book should not and could not take the place of such a course. However, these problems do serve to introduce some principles of clinical pharmacology into the usual second-year basic pharmacology course. Thus, the coordination and continuity between the second-year basic pharmacology course and the fourth-year clinical pharmacology course are strengthened.

It is our hope that students working through these problems will not only increase their knowledge of important facts and concepts, but also improve their problem-solving skills, and develop lifelong patterns of thinking wherein they apply scientific principles to clinical problems. If these goals can be accomplished in a manner that is fun, then this book will have served its purpose.

Suggestions and comments concerning this book are welcome, and can be sent to the authors at the Department of Pharmacology and Toxicology, Dartmouth Medical School, Hanover, NH 03756.

HOW TO USE THIS BOOK

We hope that as you attempt to solve the problems presented in this book, you will gain greater understanding of the basic pharmacology that you are studying. To benefit the most from these exercises, you should keep a few simple points in mind.

First, you should attempt these problems only after attending the appropriate lectures in that area and reading the suggested material from your standard pharmacology text. These problems are designed to reinforce the material that you have already studied. In addition, many of the problems assume you have had that material as background and will build from there.

Second, try to solve the problems yourself. If more information is needed, look it up yourself in an appropriate book. You must develop problem-solving skills and reference-searching skills for yourself. As you develop your answer, write it down.* Commit yourself, even if you are wrong. You will learn more if you force yourself to think through each question and commit yourself to a written answer before you compare it to the answers in this book.

Third, compare your answers closely to those suggested in the book. Were you approaching the problem in a similar fashion? Were you tripped up by lack of information, an illogical approach, or a simple arithmetic error? Can you approach the problem again in a new way after reading the suggested answer?

Fourth, never look at the answers without at least attempting to solve the problem in writing. Otherwise, you will deprive yourself of the chance to develop your problem-solving skills. Also, you may convince yourself that you really know the material, when in fact you are deluding yourself. Force yourself to commit to an answer on paper before you turn to look at the suggested answers.

Fifth, these questions and answers may be used by the individual student or by small groups of students together. Alternatively, these problems may be discussed in assigned groups during a pharmacology course. No matter how they are used, it is important for each student to attempt to solve the problems before he or she looks at the answers.

Four frequently used textbooks of basic pharmacology are cited in each chapter. To help the student move appropriately from the textbook chapter to these problems, we have keyed each chapter of problems to appropriate

*There is usually space directly following the questions.

chapters or pages in these texts (if such material is available). The full references are as follows:

Clark WG, Brater DC, and Johanson AR, editors: Goth's medical pharmacology, ed 12, 1988, St. Louis, The CV Mosby Company

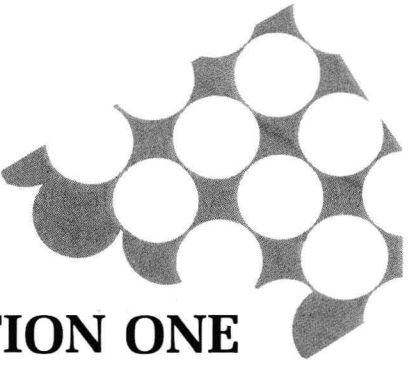
Craig CR, and Stitzel RE, editors: Modern pharmacology, ed 2, 1986, Boston, Little Brown and Company

Gilman AG, Goodman LS, Rall TW, and Murad F, editors: The pharmacological basis of therapeutics, ed 7, 1985, New York, Macmillan Publishing Company

Katzung BG, editor: Basic and clinical pharmacology, ed 3, 1987, Norwalk, Conn, Appleton and Lange

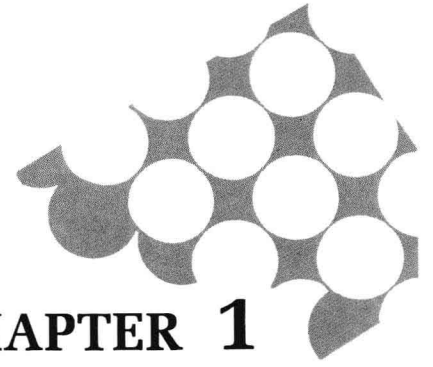
If you have a newer edition of any of the above texts, it is likely that the page numbers will differ, although the chapter headings will remain the same. Also, appropriate reading in other standard pharmacology textbooks should be easy to find simply by comparing chapter titles.

CONTENTS



SECTION ONE

GENERAL PRINCIPLES



CHAPTER 1

INTRODUCTION TO BASIC MEDICAL PHARMACOLOGY

Related Readings

Clark et al: Chapter 1, pp. 1-2; Chapter 64, pp. 758-759
Craig and Stitzel: Chapter 1, pp. 1-5
Gilman et al: Section I, Introduction, pp. 1-2; Appendix I, pp. 1561-1562
Katzung: Chapter 1, p. 1; Chapter 4, p. 50

Key Concepts

- Differences between pharmacology, toxicology, and endocrinology
- Importance of using generic names for drugs
- Differences between prescription (legend) drugs and over-the-counter (OTC) drugs

QUESTIONS

1. You are serving on the Curriculum Committee of your medical school, and are trying to decide which courses should cover the following three topics: hydrocortisone (cortisol), ethanol, and benzene. The possible courses include: basic medical pharmacology, endocrinology, and toxicology. Which topics should be covered in each course?

2. Your father is taking hydrochlorothiazide 50 mg by mouth every morning to help control his mild essential hypertension. On a follow-up visit his blood pressure is still not adequately controlled, and his physician adds HydroDIURIL™ 50 mg by mouth each day. Two weeks later his blood pressure is still not adequately controlled, and his physician adds yet another drug, Diuril™ 500 mg by mouth each day. Is such management rational?

3. Ibuprofen is a prototype, nonsteroidal anti-inflammatory drug. In the past it was available by prescription only; it was sold in 400, 600, and 800 mg tablets with the trade name Motrin™. About 2 years ago it became available for over-the-counter (OTC) purchase in the 200 mg size, and is marketed with the trade names Medipren™, Advil™, Nuprin™, and others. Why has the FDA allowed ibuprofen 200 mg to be available over the counter, but ibuprofen 400, 600, and 800 mg tablets to be available by prescription only?

ANSWERS

1. There is no one correct answer to this question. Pharmacology, endocrinology, and toxicology all deal with the effects of biologically active elements or compounds, some of which are exogenous to the patient (xenobiotics) and some of which are synthesized by the body. There are large areas of overlap among the three disciplines.

Cortisol is a glucocorticoid hormone synthesized by the adrenal glands. Thus it is appropriately considered in endocrinology. Since it is also prescribed as a drug (in physiologic and supraphysiologic dosages), it is relevant to pharmacology. Since it can produce unwanted side effects, these could be discussed in the toxicology course, although that would be stretching the definition of toxicology.

The effects of ethanol could be relevant to endocrinology since some alcoholics have ethanol-associated endocrinologic disorders. Although its legitimate therapeutic applications are now minimal (it was formerly used to stop premature labor), it is commonly covered in pharmacology. It has adverse, toxic and lethal effects germane to toxicology, and in addition may be used to treat ingestions of toxic alcohols such as methanol.

Benzene has no therapeutic uses, but it has important toxic effects on the bone marrow. Normally functioning bone marrow is under physiologic control by several hormones (for example, erythropoietin).

Some chemical entities, such as ethanol or iron, may be appropriately discussed in all three "separate" courses.

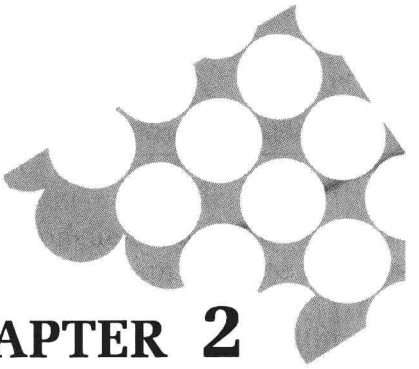
2. Hydrochlorothiazide 50 mg by mouth each day is commonly regarded as the maximal effective adult dosage of this oral thiazide diuretic used to control mild essential hypertension. Many patients are controlled by 25 mg daily. If good control of hypertension is not achieved by 50 mg per day, either another drug can be tried or another antihypertensive drug is added to the regimen.

It makes no sense to add HydroDIURIL™. If you look up this drug in a book that indexes drugs by both generic and trade names (for example, the Physician's Desk Reference or Facts and Comparisons), you will find that HydroDIURIL™ is a brand name for hydrochlorothiazide, the same drug he is taking already. Nor does it make any sense to add Diuril™, which turns out to be chlorothiazide. Chlorothiazide is in the same therapeutic class as

hydrochlorothiazide (thiazide diuretics), and offers no added benefit in a patient already taking another thiazide diuretic. Thus it is very important to know drugs by their generic names, their trade names, and their drug classes. At least it is not necessary to learn drugs by their actual chemical names.

Pharmaceutical companies can assign their own trade (proprietary) names to the drugs they manufacture, but the generic (nonproprietary) names used in the United States are assigned and approved by an official organization called the United States Adopted Names (USAN) Council, which is sponsored by the American Medical Association, the American Pharmaceutical Association, and the US Pharmacopeial Convention, in cooperation with the pharmaceutical manufacturers. Once the official USAN is adopted, that is the name that should be used to refer to a drug. If you are a student from Great Britain or Canada, you will note that some of the generic names differ between countries. For example, the opioid with the trade name Demerol™ has the generic name meperidine in the United States, and the generic name pethidine in Canada or Great Britain.

3. The FDA decides whether or not a given drug will require a prescription on the basis of whether or not the drug can be labeled in such a way that it can be used safely by the general public. We may therefore infer that the FDA decided that 200 mg ibuprofen tablets can be labeled in such a way that they can be used safely by the public, but tablets of 400 mg or more cannot. We are not privy to the actual data or line of reasoning that led to that decision. In addition to labeling concerns, the FDA also considers the abuse potential of all drugs that are considered for over-the-counter (OTC) sale.



CHAPTER 2

PHARMACEUTICAL ISSUES

Related Readings

Clark et al: Not helpful for these problems
Craig and Stitzel: Not helpful for these problems
Gilman et al: Appendix I, pp. 1652-1653
Katzung: Chapter 69, pp. 802-806

Key Concepts

- Units of mass used in modern prescriptions
- Different salts of the same active ingredient

QUESTIONS

1. Aspirin traditionally has been sold as 5 grain (gr) tablets for adults and 1.25 grain tablets for children. A middle-aged woman with severe rheumatoid arthritis has been taking 12 adult-strength aspirin tablets each day and has acheived good relief of pain and stiffness. However, her supermarket now carries a brand of aspirin that has 80 or 325 mg per tablet. How should she switch her dosage to keep taking the same amount of aspirin each day? Which units of mass are preferable, and why?