# Applied Therapeutics

The Clinical Use of Drugs

SEVENTH EDITION

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# Applied Therapeutics: THE CLINICAL USE OF DRUGS

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# Preface to the Seventh Edition

The last chapter for the seventh edition of Applied Therapeutics, Inc. (ATI) has been delivered to the publisher and we celebrate its completion. The dedication of our authors, editors, reviewers, and publisher has been remarkable and very much appreciated. Although the work on this edition now comes to a gradual close, we see much work awaiting all of us as we observe a health care system under considerable stress. Shortages of nurses, pharmacists, and other health care providers interface with remarkable new technologies, increased costs, and decreased access to care. The roles of the disadvantaged and the underserved continue to increase at a time of remarkable economic growth over the past decade. Meanwhile, health care strives to find better approaches to manage escalating costs, to enhance the quality of care provided, and to meet and exceed rising customer expectations. Systems to guarantee safety and freedom from errors (including medication errors) are urgently needed as our rapidly growing elderly populations increasingly access health care.

The future of health care ultimately resides in the next generation of practitioners. We need to recruit the best and the brightest to health care and we need to prepare them to meet the challenges of tomorrow. Our understanding of diseases has improved, new drugs are available, and we eagerly await the result of continuing research in fields such as neurochemical biology, genetics, genomics, medicine, and public health. We hope this edition shares sufficient thought processes to assist students in the formulation of the problem-solving skills needed to integrate present and future knowledge about its appropriate drug use.

All chapters in this edition have been revised and updated to reflect our changing knowledge of drugs and the application of this knowledge to the therapy of patients. As in previous editions, we have encouraged our authors to present patient cases that stimulate the reader to integrate and apply therapeutic principles to the specific patient. In this text, we have striven to provide students and practitioners with a glimpse into the minds of clinicians who are assessing and solving therapeutic problems so that they too can begin to develop their own set of problem-solving skills.

The authors have drawn much information from their clinical experiences. It remains the responsibility of every practitioner to evaluate the appropriateness of a particular opinion in the context of the actual clinical situation and with due consideration of any new developments in the field. Although the authors have been careful to recommend therapies that are in agreement with current standards and responsible literature, we recommend the student or practitioner consult several appropriate information sources when dealing with new and unfamiliar drugs.

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October 2000

# Preface to the Sixth Edition

As this sixth edition of Applied Therapeutics goes to press, unprecedented change is occurring in the delivery of health care. Managed care increasingly dictates how care will be delivered; hospitals are closing or consolidating as the number of admissions diminish and patient stays become more abbreviated; primary care providers are taking center stage, while specialists struggle to find their niche; wellness and prevention programs intended to keep patients out of health care systems are growing; and medical information systems are beginning to provide "outcomes" information for large populations. Drugs comprise approximately 7% to 9% of the total health costs and are considered by many to be one of the most cost-effective modes of treatment. Nevertheless, because drug benefits are often "carved out" of the medical reimbursement, benefit managers tend to treat these agents as commodities. Price and efficient delivery are often foremost on the minds of decision makers even though neither guarantees the desired therapeutic outcome.

This text amply demonstrates the complexity of pharmaceutical care. A good therapeutic outcome relies on the appropriate selection, use, and evaluation of drug therapy and requires thoughtful attention to the individual characteristics of the patient. As the managed care system produces an increasing number of therapeutic guidelines and clinical pathways, we urge clinicians to keep a watchful eye for the exception to the rule and to continually incorporate new data from the literature into their thinking.

Many changes have been made to this sixth edition. As in past editions, we have urged our authors to present cases which stimulate the reader to integrate and apply therapeutic principles to the specific patient described. Generous feedback from our readers caused us to expand substantially the oncology, psychiatric, derma-

tology, drug abuse, pediatric, and geriatric sections. New chapters addressing a problem-oriented approach to drug therapy and biotechnology have been added as well. For our readers outside of the United States, equivalent international units have been added, where appropriate, to the end of each case history. In addition, commonly abbreviated terms are spelled out on first usage to help familiarize practitioners with standard terminology. All chapters have been revised and updated, many of them substantially, to reflect changes in the field. We believe we have upgraded the quality of the text significantly through the critical reviews and guidance of our section editors.

Ultimately, we have added more at a time when the health care world cries for less. Nevertheless, we feel this is justified as drug therapy becomes more complex and patients previously treated in hospitals are cared for in intermediate-care facilities, the home, and other ambulatory settings. We continue to abide by the philosophies and principles set forth in the prefaces of our first and fifth editions: to provide students and practitioners with a glimpse into the minds of clinicians who are assessing and solving therapeutic problems on a daily basis so that they too can begin modeling their own problem-solving skills. The "Update Sections" we have included at the end of some chapters reaffirm our commitment to bring you a text that is as current as possible. As always, we welcome and value your comments so that we can continue to improve our product.

Lloyd Yee Young Mary Anne Koda-Kimble

August 1995

# Preface to the First Edition

In the past decade, new roles for the pharmacist have emerged. More and more frequently the pharmacist is placed in increasingly responsible positions within the health care delivery system. In this capacity (s)he is able to have a significant influence on the quality of health care delivered to the patient. M. Silverman and P. Lee have skillfully assessed the current and future role of the pharmacist in *Pills, Profits and Politics*.<sup>1</sup>

"... It is the pharmacist who can play a vital role in assisting physicians to prescribe rationally, who can help see to it that the right drug is ordered for the right patient at the right time, in the right amounts and with due consideration of costs and that the patient knows how, when and why to use both prescription and non-prescription products.

It is the pharmacist who has been most highly trained as an expert in drug products, who has the best opportunity to keep up-date on developments in this field and who can serve both physician and patient as a knowledgeable advisor. It is the pharmacist who can take a key part in preventing drug misuse, drug abuse and irrational prescribing."

Many schools of pharmacy have made substantial curriculum changes to prepare their graduates for these responsibilities. Although traditional pharmacy courses have imparted factual information about drugs, they have not enabled the students to apply these facts to the drug therapy of patients. Similarly, traditional pharmacology and medical text books do not provide the professional with sufficient information to make a judgment regarding the selection and dosing of a particular product for a specific patient. To arrive at this decision, the clinician must consider a number of patient factors, including age, renal and hepatic function, concurrent disease states and medications and allergies. (S)he must also consider drug product factors, including bioavail-

ability, pharmacokinetics, efficacy, toxicity, risk to benefit ratio, and cost.

We have found that students who have most difficulty in *integrating* and *applying* the multiple components of their education to formulate the safest, most rational drug regimen for a given patient. We have also observed that although the student is able to enumerate the adverse effects on a drug, (s)he is unable to recognize or monitor for these effects should they occur in his/her patient.

This text is an outgrowth of the clinical pharmacy courses taught at the University of California and at Washington State University. The major objective of these courses is to enable the student to practice effectively in the clinical setting. Lectures on the pathophysiology and medical management of disease states are supplemented with conferences where students are challenged with drug therapy questions frequently asked by physicians and by case histories which require drug therapy assessment and the selection of appropriate alternatives. The objective of these conferences and this text is to enable the student to identify relevant factors in drug treatment, such as the probability of whether or not a specific drug is responsible for a patient's symptoms; the clinical significance of a drug interaction; why a specific drug is not achieving therapeutic blood levels; the dose for a patient with multiple disease states.

The success of the conference portion of our courses was a major determinant of the format used for this text; case histories which simulate the actual practice situations and frequently asked therapeutic questions are followed by well-referenced responses.

The authors have drawn much information from their clinical experiences. It remains the responsibility of every practitioner to evaluate the appropriateness of a particular opinion in the context of the actual clinical situation and with due considerations of any new developments in the field. Although the authors have been careful to recommend dosages that are in agreement with current standards and responsible literature, we suggest the student or practitioner consult several appropriate information sources when dealing with new and unfamiliar drugs.

<sup>&</sup>lt;sup>1</sup>Silverman, M. and Lee, PR.: Pills, Profits and Politics, University of California Press, Berkeley, 1975, p. 192.

# **Acknowledgments to Seventh Edition**

We are deeply indebted to the many dedicated people who have given of themselves to complete the seventh edition of this book. As always, we are grateful to our contributing authors who struggled not only with deadlines and format, but also with significant changes in the management of our publication team. We thank the section editors for their truly remarkable support as they edited chapters, assisted authors, and assisted us in the changeover from Applied Therapeutics, Inc. to Lippincott Williams & Wilkins (LWW). More specifically, thank you to section editors Brian K. Alldredge (Neurologic Disorders), Jeffrey N. Baldwin (Substance Abuse), Ann Bolinger-Churukian (Pediatrics), Thomas J. Comstock (Renal Disorders), Allan J. Ellsworth (Dermatologic Disorders), Beverly J. Holcombe (Nutrition), Celeste M. Lindley (Neoplastic Disorders), Mark D. Watanabe and Patrick R. Finley (Psychiatric Disorders), and Bradley R. Williams (Geriatric Therapy).

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B. Joseph Guglielmo Mary Anne Koda-Kimble Wayne A. Kradjan Lloyd Yee Young

October 2000

# **Notice to Reader**

Drug therapy information is constantly evolving. Our everchanging knowledge and experience with drugs and the continual development of new drugs necessitates changes in treatment and drug therapy. The editors, authors, and publisher of this work have made every effort to ensure the information provided herein was accurate at the time of publication. It remains the responsibility of every practitioner to evaluate the appropriateness of a

particular opinion or therapy in the context of the actual clinical situation and with due consideration of any new developments in the field. Although the authors have been careful to recommend dosages that are in agreement with current standards and responsible literature, the student or practitioner should consult several appropriate information sources when dealing with new and unfamiliar drugs.

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