英文影印版

Fourth Edition

药物治疗学

PHARMACOTHERAPY

Volume 2

第4版 下册

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科学出版社

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科 学 出 版 社
McGraw-Hill
2000

Joseph T. Dipiro, Robert L. Talbert, Gary C. Yee, Gary R. Matzke, Barbara G. Wells, L. Michael Posey: Pharmacotherapy, Fourth Edition

IE ISBN 0-07-1187707

图书在版编目(CIP)数据

药物治疗学＝Pharmacotherapy：英文影印版/(美)迪彼罗(Dipiro, J. T.)主编．-4版．-北京：科学出版社，2000.9

ISBN 7-03-008734-8

Ⅰ.药… Ⅱ.迪… Ⅲ.药物疗法-英文 Ⅳ.R453

中国版本图书馆CIP数据核字(2000)第67541号

北京市版权局版权登记号：图字01-2000-1761

科学出版社 出版
北京东黄城根北街16号
邮政编码：100717

新蕾印刷厂印刷

科学出版社发行 各地新华书店经销

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2000年9月第 一 版 开本：787×1092 1/16
2000年9月第一次印刷 印张：155 3/4
印数：1—3 000 字数：5 482 000

定价：330.00元(上、下册)

(如有印装质量问题，我社负责调换〈杨中〉)

FOREWORD

We are in the midst of rapid changes as the 20th century comes to a close. Although these rapid changes are occurring in all aspects of our lives, the dynamic changes in health care have startled all health professionals. Not too long ago we had a clear and unquestioned goal of the highest possible quality of care for our patients. But as the cost of patient care increased significantly in excess of the costs of other goods and services, the concept of managed health care was developed. Some critics state that managed health care is, in reality, managed health costs, whereas supporters state that quality care can be achieved while being cost conscious. However, both critics and supporters of managed health care agree that the practices of clinicians will continue to be influenced by increased cost consciousness in health care reimbursed through both private and public programs. This is particularly the case in the area of pharmacotherapy.

We are also in a time when great advances in biomedical research are catalyzing the development of important new drugs that, in some cases, treat diseases that previously had no treatment, and in other cases, greatly improve upon previous therapies. But in some cases new drugs may not have benefits over older therapies that justify the often higher costs of the new therapy. The challenge is to welcome new drug therapies that are necessary for quality patient care and to reject those drug therapies that merely add cost without improving quality of care. Moreover, managed health care executives must realize that drug therapy, even when appearing expensive, is almost always the least costly alternative for patient care.

Just as rapid changes are occurring in health care and in drug therapies, rapid changes are also occurring in the profession of pharmacy. One hundred years ago pharmacists were compounders of prescriptions—a role now dominated by pharmaceutical manufacturers. Forty years ago pharmacists were primarily distributors of prescription drugs—a role of limited professional responsibility today. In 1966 Dean Linwood F. Tice of the Philadelphia College of Pharmacy stated,

> "I predict that the counting and pouring now often alleged to be the pharmacist's chief occupation will in time be done by technicians and eventually by automation. The pharmacist of tomorrow will function by reason of what he knows—increasing the efficiency and safety of drug therapy and working as a drug specialist in his own right. It is in this direction that pharmaceutical education must move without delay."

I was a faculty member at the Philadelphia College of Pharmacy in 1966 and I participated in Dean Tice's efforts to move pharmacy in a clinical direction toward what we now call pharmaceutical care.

Later, at the University of Kentucky, and for 20 years at the University of Texas, I had the good fortune to be a colleague and friend of Charles Walton. Charlie Walton wrote the Foreword to the first edition of this textbook. His Foreword eloquently addressed the importance of pharmacotherapy in the maturing of the profession of pharmacy. Charlie stated,

> "Within this book one will find the scientific foundation for the essential knowledge required of one who may aspire to specialty practice as a pharmacotherapist."

Note that Charlie stated, ". . . scientific foundation for the essential knowledge . . ." One thing Charlie Walton taught me was that the clinical pharmacy specialists he wanted to educate and train could not take any short cuts—the pharmacotherapist had to be a clinician who had a strong scientific foundation.

When we conceived our Texas clinical program in 1973, we committed to a three year post-baccalaureate PharmD program with an integrated residency program. These students took pathophysiology, along with medical students. No short cuts. The Texas PharmD program has evolved along with the adoption of the PharmD as the only professional degree in pharmacy. The principles that existed in the 1970s in a few schools have now generally been adopted by all colleges of pharmacy. However, specialty practice as a pharmacotherapist continues to require graduate pharmacy education beyond the PharmD, just as specialty practice in medicine requires graduate medical education beyond the MD. This text continues to be intended as "the scientific foundation for the essential knowledge required of one who may aspire to specialty practice as a pharmacotherapist."

It is interesting that Charlie Walton often stated that he was not a clinical pharmacist. I questioned his self-assessment because, in my view, he was a uniquely talented leader and motivator for patient-oriented concepts in pharmacy education and practice. However, Charlie Walton had very high standards for a pharmacist to be termed a clinical pharmacist or a pharmacotherapist. These standards should remain high as opportunities continue to expand for pharmacotherapists to enter one-on-one, collaborative practice with physicians and other health professionals. High standards will ensure the level of clinical competence needed in the pharmacotherapist to earn the respect of patients and medical colleagues.

William Miller wrote the Foreword in the second edition of *Pharmacotherapy*. Bill is a pioneer—a first generation clinical pharmacist and pharmacotherapist. He earned his PharmD at the University of Kentucky when Charlie Walton and I were on faculty. There were no pharmacy precedents for the education and training Bill received and there was no roadmap for him to follow in his career. Therefore, it was with a teacher's pride that I read his Foreword to the second edition. Bill's Foreword had

the orientation of a practitioner that knew our recent successes in the evolution of pharmacotherapists are only a beginning. We have successfully demonstrated potential; the continuing challenge will be to broadly improve patient care through the specialty practice of more, and better trained, pharmacotherapists. Bill stated,

> "All pharmacotherapists additionally must document the effects of their actions on patient drug therapy outcomes. The relative value of Pharmacotheraphy Specialists in terms of costs and benefits must be compared with those of other professionals and technology, all these costs are driving up the price of health care. We must be avid supporters of continuous quality improvement which will encourage decisions about health care delivery systems based on fact and not simply opinion or perceptions."

In the Foreword to the third edition, Milo Gibaldi stated,

> "The idea of pharmaceutical care continues to enjoy near universal support in the profession, yet we have had critical lapses in organizational and academic leadership."

Practice as a clinical pharmacy specialist is no longer an experiment or pilot project. It has become a valued practice enhancing patient care. The time has come for a full commitment of organizational and academic leadership to the advancement of high quality clinical pharmacy specialty practice as well as the advancement of general practice oriented to pharmaceutical care. Strong leadership and a careful strategy will be required to advance the general and specialty practices of pharmacy in ways that do not advance one type of practice at the expense of the other.

The fourth edition of this textbook is strong evidence that the profession of pharmacy is continuing its exciting progress as a clinical profession. This text could not have been written in 1966. There were not pharmacists who could have authored the material, nor were there reasonable opportunities for pharmacists to utilize the material in practice even if, somehow, the book were authored. Today we have both the authors and the opportunity to improve patient care.

I hope that someday in the future, a leading pharmacotherapist will look back at this text and judge it to be "the text" that made the difference in pharmacists truly becoming pharmacotherapists. That is how I view the text. As dean of pharmacy at the University of Texas from 1973 to 1998, I participated, along with Charlie Walton, Bob Talbert, and others, in the development of faculty and programs that were based on pharmacy being a clinical profession. Other colleges and institutions made similar commitments. I look at this text as evidence that through these efforts the profession of pharmacy has joined medicine, nursing, and dentistry as a clinical profession.

We are in the midst of a wonderful journey.

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February 1999

PREFACE

The publication of the fourth edition of *Pharmacotherapy: A Pathophysiologic Approach* continues the standards and philosophies set forth by the previous editions. *Pharmacotherapy* seeks to advance the level of pharmaceutical care through understanding of pharmacotherapeutic principles. We believe that this textbook will stimulate the pharmacy student to achieve a higher level of learning; motivate the young practitioner to perform more advanced patient care; challenge established pharmacists to learn concepts missed during years of practice; and inform the profession at large about the standards of pharmaceutical care toward which all should strive.

The authors and editors have attempted to impart a process of thinking about pharmacotherapy for the student and developing practitioner. The key to this process is the pathophysiology sections, which identify mechanisms of disease as a foundation for applying pharmacotherapeutic principles and strategies. By understanding pathophysiology and principles of therapy, the student and practitioner can assess more rigorously the place of new drugs or new therapeutic approaches.

In this edition, we have reached the limits of text that can be included in one volume and therefore made carefully considered decisions on chapters to be added and deleted. The present edition includes 132 chapters, an overall reduction of four chapters from the third edition. *New chapters* have been added on "Disorders of the Pituitary Gland" and "Substance-Related Disorders."

The *structure* of chapters and *design* of pages has continued to evolve to better meet user needs. In this edition, the following new features have been included: **more structured treatment sections**, containing a different type face which sets off the material in a visual way (**see example below**), a new section on **desired outcomes** of treatment, **redrawn flow diagrams**, disease states end-of-chapter reminders titled **principles of pharmacotherapy** which put the major points in perspective.

The overall organization of the book is retained from previous editions. The first seven chapters again provide *primers* on important fundamental information such as: **pharmacoeconomics, pharmacoepidemiology, pharmacokinetics, drug interactions,** and **clinical toxicology.**

Most of the remaining chapters specifically focus on disease states and maintain a *standard format* which includes the following headings: **epidemiology, pathophysiology, clinical presentation, desired outcomes, treatment,** and **evaluation of therapeutic outcomes.**

The textbook together with its companion works, *Pharmacotherapy Casebook: A Patient-focused Approach, Pharmacotheraphy Handbook,* and the *Pharmacotherapy.complete* CD-ROM provide a comprehensive package of tools useful for practice and instruction. New editions of each of the companion products should be available about the time that the fourth edition is published.

The editors recognize that many areas of this text will rapidly become outdated as our understanding of disease processes increases or as new therapies are adopted. The challenge for the student and the practitioner is to integrate information from a variety of sources, form a basis for application in pharmacotherapy, and be receptive to new information as it appears in the literature or as it is gained by personal experience.

The editors are deeply indebted to the contributors for the hours spent preparing accurate, thorough, and relevant discussions of each topic. A heartfelt thank you is well earned by the personnel at Appleton & Lange, especially Cheryl Mehalik, who provided critical support, insight, and motivation at every stage.

The Editors
April 1999

Example:

▶ TREATMENT: Syndrome X

Syndrome X refers to the occurrence of effort angina and exercise-induced ECG changes with a normal coronary arteriogram with no evidence of structural (stenosis) or functional (spasm) abnormalities. Although the basis for this syndrome is not yet established, it is thought that syndrome X may be a result of inducible myocardial ischemia caused by impaired functional coronary reserve at the microvascular level of intramural prearteriolar vessels. It has been proposed that this defect is caused by defective prearteriolar regulation of blood flow into the arteriolar bed with subsequent focal, sustained, compensatory release of adenosine; excessive local concentrations of adenosine are then responsible for the pain seen in this syndrome. Prearteriolar constriction may be the result of insufficient vasodilation or inappropriate vasoconstriction, or resetting of myogenic control on a segmental or generalized distribution basis.

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GUIDING PRINCIPLES OF PHARMACOTHERAPY

1. There should be a justifiable indication for every medication that a patient receives.
2. A medication should be used at the lowest dosage and for the shortest duration that is likely to achieve the desired outcome.
3. Do not use more than one medication when one alone will be adequate.
4. Newly approved medications should be used only if there are clear advantages over older medications.
5. Whenever possible, the selection of a medication regimen should be based on evidence obtained from controlled clinical trials.
6. The timing of drug administration should be considered as a possible influence on drug efficacy, adverse effects, and interactions with other drugs and food.
7. A medication regimen should be simplified as much as possible to enhance patient compliance.
8. A patient's perception of illness or the risks and benefits of therapy should be recognized as possibly affecting compliance and treatment outcomes.
9. Careful observation of a patient's response to treatment is necessary to confirm efficacy, prevent, detect, or manage adverse effects, assess compliance, and determine the need for dosage adjustment or discontinuation of drug therapy.
10. To enhance compliance, choose a medication regimen that the patient can afford.
11. A medication should not be given by injection when giving it by mouth would be just as effective and safe.
12. Before medications are used, lifestyle modifications should be made, when indicated, to obviate the need for drug therapy or enahance pharmacotherapy outcomes.
13. Initiation of a drug regimen should be done with full recognition that a medication may cause a disease, sign, symptom, syndrome, or abnormal laboratory test.
14. When a variety of drugs are equally efficacious and equally safe, the drug which results in the lowest health care cost or is most convenient for the patient should be chosen.
15. When making a decision about drug therapy for individual patients, societal effects should be considered.
16. It is important to recognize the possible reasons for failure of medication regimens, which include poor compliance, improper drug dose or interval, misdiagnosis, concurrent illness, interactions with foods and drugs, environmental factors, or genetic factors.

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August 17, 1998

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