Drug Interactions in Infectious Diseases
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Drug Interactions in Infectious Diseases

Second Edition

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Foreword by

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Over the past 25 years, the world’s population has witnessed an explosion in knowledge about infectious diseases. The global population is coming to the realization that diseases long recognized to cause substantial suffering, such as malaria, tuberculosis, schistosomiasis, and hepatitis, can be diagnosed and treated, and that transmission can be prevented using tools that are available, and which may be becoming increasingly affordable. The global population is recognizing that few infections are local: the travel of humans, other animals, insects, and food transport pathogens around the world, often with astonishing rapidity. New pathogens are appearing, either newly recognized or newly developing, such as severe acute respiratory syndrome (SARS), avian influenza, metapneumovirus, or hepatitis C, which are causing human morbidity and mortality. Finally, there is growing fear that dangerous pathogens may be intentionally introduced into human populations by deranged individuals or terrorist organizations.

The potential to use drugs or biologic agents to treat and prevent infectious diseases has increased dramatically over the past quarter century as we have learned more about the biology of many of these agents, and as we have developed techniques to discover new agents by high throughput screening programs and by sophisticated drug design and synthesis. The development of more than 20 licensed drugs for therapy of HIV infection within 20 years of discovering the etiologic retrovirus is a prime example of the extraordinary capacity the scientific community has to produce safe and effective agents. New drugs to treat hepatitis C, hepatitis B, influenza, staphylococci, enterococci, plasmodia, flukes, candida, and molds also demonstrate the impressive potential the health care industry has to produce new agents.

For all clinicians, it is clear that the scientific advances in understanding pathogenesis of infectious diseases, and in developing new diagnostic tests, new therapeutic agents, and new preventive strategies have made management of diseases both impressively more successful and yet immensely more complex. It is also clear that non-infectious diseases are being managed more successfully with pharmacologic interventions, such that patients may be on multiple agents to treat related or unrelated processes, and to prevent processes, when they develop an acute or chronic infection that needs to be treated. Patients are not uncommonly on drugs for diabetes, lipid disorders, cardiac dysfunction, or inflammatory disorders. In the United States, more and more individuals have altered their dietary habits substantially to reduce weight or improve some other aspect of their health. These diets, or nonprescription drugs or supplements used in the United States or abroad, can have substantial impact on drug pharmacokinetics.

Though therapy with drugs or biologic agents can be highly effective, many factors influence the efficacy and safety of therapy, including adherence, absorption, metabolism, excretion, and drug interactions. Interactions may occur between or among drugs used specifically for treating the infection, such as interactions between two
antiretroviral agents or interactions between rifampin and quinolones or macrolides. Such interactions can be used for therapeutic advantage, such as the interaction between ritonavir and other protease inhibitors, or these interactions may be potentially harmful, as the interaction between didanosine and stavudine. Interactions may occur between drugs used to manage the infectious disease, and drugs used to manage unrelated problems, such as the interaction between coumadin or phenytoin and ritonavir. Some of the outcomes can be highly undesirable, such as the interaction between rifampin and oral contraceptives. Lastly, interaction can occur between nutritional substances or nonprescription drugs and antiinfectives, such as the interaction between garlic or St. John’s Wort or Echinacea and protease inhibitors.

The first edition of *Drug Interactions in Infectious Diseases* became an important reference for all health care practitioners, and not only pharmacists, since all needed specific data on how to prescribe multidrug regimens in a manner that maximized efficacy and minimized toxicity. The second edition has been revised and updated. The chapter on mechanisms of drug interactions has been expanded into two chapters to allow increased description of absorption, metabolism, and excretion, and to describe the growing knowledge about transport proteins. A useful chapter on regulatory issues including CYP450 probe studies has also been added.

Stephen Piscitelli, PharmD, and Keith Rodvold, PharmD have been pioneers and leaders in recognizing the importance of drug interactions to patient outcome. They have been leaders in designing pharmacokinetic studies that can answer both conceptual questions and practical problems. Most importantly, however, they have recognized the need for health care professionals to have a well organized, definitive source of information to enhance patient care. Safe and effective care for patients is becoming an increasingly complex task best performed by well-trained health care professionals who know how to access data that is vital to their management strategy. The approach to drug interactions described in *Drug Interactions in Infectious Diseases, Second Edition*, and the factual information presented are an essential part of the resources needed to maximize the likelihood that patients will derive the most benefit from available drugs with the least likelihood of harm.

*Henry Masur, MD*
Preface

Drug interactions in the field of infectious diseases continue to expand as new drugs are approved, new mechanisms are identified, and recommendations for co-administration of drugs are revised. The editors of *Drug Interactions in Infectious Diseases* are gratified that the first edition was well received and we are enthusiastic about the additions and improvements to this second edition.

Major changes have taken place in our understanding of interaction mechanisms. The literature on P-glycoprotein and other transporters has dramatically increased since the first edition. There is so much new knowledge on transport proteins that an entire chapter has been devoted to this issue. We have also included a chapter outlining the regulatory perspective on interaction studies in drug development since guidances from various countries have been put forth. In addition to these new chapters, our authors have updated their chapters to include new drugs that have become available since the first edition. This is especially true in the field of HIV infection, where several new drugs have been approved over the past three years. Finally, the aspects of this text that make it unique are once again present. The chapter on study design and data analysis is one of the best of its kind. New cases have been added to each chapter and highly acclaimed chapters, such as food interactions and drug–cytokine interactions, are updated and revised.

We feel strongly that *Drug Interactions in Infectious Diseases* has something to offer everyone working in the field of infectious diseases. The practicing clinician, academician, or researcher will all find this book useful. The information contained within here ranges from detailed tables on specific drug–drug interactions to in-depth discussions of mechanisms and research issues.

We would again like to thank our excellent group of authors who have devoted so much time into making this more than just a reference book. Their commitment to this textbook clearly shows. Finally, we could not complete such an undertaking without the support of our families who have encouraged us throughout.

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