
The
Quinolones
THIRD EDITION
Edited by
VINCENT T. ANDRIOLE

THE QUINOLONES

Third Edition

Edited by

VINCENT T. ANDRIOLE

Yale University School of Medicine

ACADEMIC PRESS

San Diego London Boston New York Sydney Tokyo Toronto

This book is printed on acid-free paper. ∞

Academic Press
a Harcourt Science and Technology Company
525 B Street, Suite 1900, San Diego, California 92101-4495

http://www.academicpress.com

Academic Press Limited
Harcourt Place, 32 Jamestown Road, London NW1 7BY, UK

Library of Congress Catalog Card Number: 00-106606

International Standard Book Number: 0-12-059517-6

PRINTED IN UNITED STATES OF AMERICA
02 03 04 05 SB 9 8 7 6 5 4

Compliments of Bayer Corporation, Pharmaceutical Division,

maker of

Compliments of Bayer Corporation, Pharmaceutical Division, maker of Avelox® (moxifloxacin HCl) Tablets, Avelox® I.V. (moxifloxacin HCl in NaCl Injection), Cipro® (ciprofloxacin HCl) Tablets, Cipro® (ciprofloxacin) 5% and 10% Oral Suspension, and Cipro® I.V. (ciprofloxacin).

These medications are indicated for treatment of the following infections when due to susceptible strains of indicated pathogens:

Avelox® Tablets and *I.V.*: acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, community-acquired pneumonia, and uncomplicated skin and skin structure infections.

Cipro® Tablets, Cipro® Oral Suspension, and *Cipro® I.V.*: acute sinusitis; lower respiratory tract infections; nosocomial pneumonia (I.V. only); urinary tract infections; acute uncomplicated cystitis in females (Tablets and Oral Suspension only); chronic bacterial prostatitis; complicated intra-abdominal infections (in combination with metronidazole); skin and skin structure infections; bone and joint infections; infectious diarrhea, typhoid fever (enteric fever) and uncomplicated cervical and urethral gonorrhea (Tablets and Oral Suspension only); and inhalational anthrax (post-exposure) to reduce the incidence or progression of disease following exposure to aerosolized *B anthracis*.*

Cipro® I.V. also is indicated as empirical therapy for febrile neutropenic patients (in combination with piperacillin sodium).

Other uses discussed in this textbook have not been approved by the FDA.

The safety and effectiveness of Cipro and Avelox in children, adolescents less than 18 years of age, except for inhalational anthrax (post-exposure) with Cipro, pregnant women, and lactating women have not been established.

NOTE: Although effective in clinical trials, ciprofloxacin is not a drug of first choice in the treatment of presumed or confirmed pneumonia secondary to *S pneumoniae.*

*Ciprofloxacin serum concentrations achieved in humans serve as a surrogate endpoint reasonably likely to predict clinical benefit and provide the information for this indication.

Bayer
Pharmaceutical Division
Bayer Corporation
400 Morgan Lane
West Haven, CT 06516

B07021 BAY-0021 12/01

To my family
who have supported and
encouraged me always
and in everything.

To my colleague, Susan Marino,
who has assisted me in
all professional activities.

CONTRIBUTORS

Numbers in parentheses indicate the pages on which the author's contribution begin.

VINCENT T. ANDRIOLE (255, 477), Yale University School of Medicine, New Haven, Connecticut 06520-8022

PETER BALL (1), School of Biomedical Sciences, University of St. Andrews, St. Andrews, Fife KY16 9AL, Scotland, United Kingdom

KAREN BRASEL (285), Department of Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin 53226

KATHERINE E. BRIGHTY (33), Department of Medicinal Chemistry, Central Research Division, Pfizer Inc., Groton, Connecticut 06340

RICHARD P. DiCARLO (227), Department of Medicine, Louisiana State University School of Medicine, New Orleans, Louisiana 70112

SEBASTIAN FARO (285), Department of Obstetrics and Gynecology, Rush Medical College, Rush Presbyterian and St. Luke's Medical Center, Rush University, Chicago, Illinois 60612

THOMAS D. GOOTZ (33), Department of Respiratory, Allergy, Immunology, Inflammation, and Infectious Diseases, Central Research Division, Pfizer Inc., Groton, Connecticut 06340

SHERWOOD L. GORBACH (303), Department of Community Health, Tufts University School of Medicine, Boston, Massachusetts 02111

DAVIDSON H. HAMER (303), Division of Geographic Medicine and Infectious Diseases, Department of Medicine, New England Medical Center, Boston, Massachusetts 02111

RODRIGO HASBUN (325), Tulane University School of Medicine, Section of Infectious Diseases, New Orleans, Louisiana 70118

PAUL B. IANNINI (255), Department of Medicine, Danbury Hospital, Danbury, Connecticut 06810, and Yale University School of Medicine, New Haven, Connecticut 06520

ADOLF W. KARCHMER (371), Division of Infectious Diseases, Beth Israel Deaconess Medical Center, and Harvard Medical School, Boston, Massachusetts 02215

MYO-KYOUNG KIM (169), Department of Pharmacy and Division of Infectious Disease, Hartford Hospital, Hartford, Connecticut 06102-5037

ANNA KING (99), Department of Microbiology, United Medical and Dental School of Guy's and St. Thomas' Hospitals, St. Thomas' Hospital, London SE1 7EH, United Kingdom

THILO KÖHLER (139), Department of Genetics and Microbiology, University of Geneva, 1211 Geneva, Switzerland

HARTMUT LODE (397), Department of Chest and Infectious Diseases, Hospital Zehlendorf, Heckeshorn Lung Clinic, 14109 Berlin, Germany

DAVID H. MARTIN (227), Department of Medicine, Louisiana State University School of Medicine, New Orleans, Louisiana 70112

LINDSAY E. NICOLLE (203), Department of Internal Medicine, University of Manitoba, Winnipeg, Manitoba, R3A 1R9, Canada

MICHAEL S. NIEDERMAN (255), Division of Pulmonary and Critical Care Medicine, Winthrop-University Hospital, Mineola, New York 11501, and Department of Medicine, State University of New York at Stony Brook, Stony Brook, New York 11794

CHARLES H. NIGHTINGALE (169), Office of Research Administration, Hartford Hospital, Hartford, Connecticut 06102-5037

JEAN-CLAUDE PECHÈRE (139), Department of Genetics and Microbiology, University of Geneva, 1211 Geneva, Switzerland

IAN PHILLIPS (99), Department of Microbiology, United Medical and Dental School of Guy's and St. Thomas' Hospitals, St. Thomas' Hospital, London SE1 7EH, United Kingdom

VINCENT J. QUAGLIARELLO (325), Section of Infectious Diseases, Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut 06520-8022

KENNETH V. I. ROLSTON (343), Department of Medical Specialties, Section of Infectious Diseases, The University of Texas, M. D. Anderson Cancer Center, Houston, Texas 77030

URS B. SCHAAD (455), Department of Pediatrics, University of Basel, 4058 Basel, Switzerland

KEVIN SHANNON (99), Department of Microbiology, United Medical and Dental School of Guy's and St. Thomas' Hospitals, St. Thomas' Hospital, London SE1 7EH, United Kingdom

RALF STAHLMANN (397), Department of Pharmacology and Toxicology, Institute of Clinical Pharmacology and Toxicology, University Hospital Benjamin Franklin, Freie Universität Berlin, 14195 Berlin, Germany

JOHN WEIGELT (285), Department of Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin 53226

PREFACE

Substantial progress has been made in the development of newer quinolones since the last edition of *The Quinolones* was published. This progress occurred because the quinolone class of antibacterial agents has captured the interest of chemists, microbiologists, pharmacologists, and clinicians. Recent progress in molecular biology has provided new information and a better understanding of structure–activity relationships of the quinolone nucleus and its radicals. This progress has resulted in the approval of a few new compounds with improved mechanism of action and the potential for delaying the development of resistance by specific bacterial pathogens. A few of the newest quinolones developed recently—moxifloxacin, gatifloxacin, and gemifloxacin—provide a more potent spectrum of activity that includes penicillin-resistant pneumococci as well as good activity against anaerobes and decreased susceptibility to the development of resistance by some bacterial species. Trovafloxacin was the first quinolone that demonstrated improved penetration into the central nervous system and cerebrospinal fluid, and early clinical studies demonstrated excellent efficacy in pediatric patients with bacterial meningitis. The newest quinolones—moxifloxacin, gatifloxacin, and gemifloxacin—broaden the clinical utility of this class of antimicrobial agents as we enter an era of increasing bacterial resistance to the previously recommended "standard therapy." During this same period, we have learned much about quinolone toxicity as it relates to quinolone chemical structure and pharmacokinetics/pharmacodynamics in treated patients. Hopefully this knowledge will provide safer molecules for use in patients.

The excellent and very recent progress that has occurred warranted an update on the quinolones. This edition is intended to provide the newest and most cogent information on the quinolones—all of it readily available in one volume.

Once again, I am much indebted to my colleagues, each of whom contributed thorough reviews on the history, chemistry, and mechanism of action, *in-vitro* properties, mechanisms of bacterial resistance, pharmacokinetics, clinical overview (described in nine separate chapters, including pediatrics), toxicity, adverse effects and drug interactions, and the future prospects of the newer quinolones.

Clearly, our hope is that this work will serve as a ready resource for new and helpful information, and, in so doing, the efforts of my colleagues most certainly will have been worthwhile.

Vincent T. Andriole
Yale University School of Medicine

CONTENTS

10 Use of the Quinolones for Treatment and Prophylaxis of Bacterial Gastrointestinal Infections

Davidson H. Hamer and Sherwood L. Gorbach

11 Use of the Quinolones in Treatment of Bacterial Meningitis

Rodrigo Hasbun and Vincent J. Quagliarello

12 Use of the Quinolones in Immunocompromised Patients

Kenneth V. I. Rolston