

Leading article

Role of newer fluoroquinolones in lower respiratory tract infections

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The impact of respiratory infections on individuals in society is important and is growing as the population ages. Lower respiratory tract infections in particular are major causes of morbidity and mortality. These infections include acute exacerbation of chronic bronchitis (AECB) and community-acquired pneumonia. Of the two conditions, AECB is more prevalent, occurring in 46% of the population over 65 years old in Germany, with an average of 2.4 acute exacerbations per patient each year. In the UK, chronic bronchitis causes 5% of deaths and is responsible for 28 million lost working days per year.

Community-acquired respiratory tract infections (RTIs) may be caused by Gram-positive organisms (predominantly *Streptococcus pneumoniae*), Gram-negative organisms (*Haemophilus influenzae* and *Moraxella catarrhalis*) and 'atypical' bacteria (e.g. *Chlamydia pneumoniae*, *Legionella pneumophila* and *Mycoplasma pneumoniae*). In community-acquired pneumonia (CAP) pathogens, penicillin resistance has emerged worldwide among pneumococci, while β -lactamase production among *H. influenzae*, *M. catarrhalis* and many Gram-negative bacilli has led to alterations in first-line therapy options.

Although the quinolone class of drugs has been in existence since 1962, only since the fluorination of the molecule in 1983 has the class been considered a major antibacterial group. The classic fluoroquinolones such as ciprofloxacin, norfloxacin, fleroxacin and ofloxacin have had strong activity against Gram-negative bacteria, but the effectiveness of these compounds against Gram-positive bacteria has been debated. The fluoroquinolones developed during the 1990s, notably levofloxacin, gatifloxacin, moxifloxacin and gemifloxacin, have demonstrated enhanced activity against the most common bacteria involved in lower respiratory tract infection (LRTI). The mechanism of newer fluoroquinolone activity is the inhibition of essential bacterial type II topoisomerases (DNA gyrase) and topoisomerase IV. The *in vitro* antibacterial

activity of all new fluoroquinolones against respiratory pathogens is excellent (Table 1). *S. pneumoniae* MIC₉₀s are reported to be from 0.016 (gemifloxacin) to 0.25 mg/L for moxifloxacin, 0.5 mg/L for gatifloxacin and 1–2 mg/L for levofloxacin. This activity also includes penicillin- and macrolide-resistant pneumococci. New fluoroquinolones are highly active against *H. influenzae* and *M. catarrhalis*, with MIC₉₀s < 0.1 mg/L. In addition, against atypical pathogens the MIC₉₀s are usually <0.125 mg/L for all substances.¹

Pharmacokinetic/pharmacodynamic properties of fluoroquinolones are important factors to consider, as they have a significant impact on clinical efficacy and safety (Table 2). All new fluoroquinolones have a bactericidal activity and a post-antibiotic effect. Compared with ciprofloxacin, all new fluoroquinolones have a longer elimination half-life that allows once daily dosing. In addition, these antibiotics have excellent penetration into respiratory tissues, with the highest concentrations found in the epithelial lining fluid and alveolar macrophages.² Both locations are important for extracellularly and intracellularly growing pathogens. The newer fluoroquinolones gatifloxacin, levofloxacin and moxifloxacin are currently available, or will be in the near future, in both iv and oral formulations. Gatifloxacin and moxifloxacin reach similar plasma concentrations with both formulations when administered in equivalent doses to levofloxacin. Physicians may thus have greater flexibility to use all formulations in seriously ill patients, who would normally have to exclusively receive iv therapy.³

With regard to the pharmacodynamic characteristics, the new fluoroquinolones cause concentration-dependent killing. For this category of antibiotics, peak serum concentrations, i.e. C_{max} and AUC, are important parameters for accessing clinical response. *In vitro* studies have shown that a C_{max}:MIC ratio of >10 prevents the emergence of antimicrobial-resistant microorganisms and also favours a positive clinical outcome. The ratio of the AUC over 24 h above the MIC₉₀ (AUC)

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Chao Zhang



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Kucers' The Use of Antibiotics Sixth Edition M Lindsay Grayson, Suzanne M Crowe, James S McCarthy, John Mills, Johan W Mouton, S Ragnar Norrby, David L Paterson, Michael A Pfaller, 2010-10-29 I am unaware of any textbook which provides such comprehensive coverage of the field and doubt that this work will be surpassed in the foreseeable future if ever From the foreword by Robert C Moellering Jr M D Shields Warren Mallinckrodt Professor of Medical Research Harvard Medical School USA Kucers The Use of Antibiotics is the leading major reference work in this vast and rapidly developing field More than doubled in length compared to the fifth edition the sixth edition comprises 3000 pages over 2 volumes in order to cover all new and existing therapies and emerging drugs not yet fully licensed Concentrating on the treatment of infectious diseases the content is divided into 4 sections antibiotics anti fungal drugs anti parasitic drugs and anti viral drugs and is highly structured for ease of reference Within each section each chapter is structured to cover susceptibility formulations and dosing adult and paediatric pharmacokinetics and pharmacodynamics toxicity and drug distribution detailed discussion regarding clinical uses a feature unique to this title Compiled by an expanded team of internationally renowned and respected editors with a vast number of contributors spanning Europe Africa Asia Australia South America the US and Canada the sixth edition adopts a truly global approach It will remain invaluable for anyone using antimicrobial agents in their clinical practice and provides in a systematic and concise manner all the information required when treating infections requiring antimicrobial therapy Kucers The Use of Antibiotics is available free to purchasers of the books as an electronic version on line or on your desktop It provides access to the entire 2 volume print material It is fully searchable so you can find the relevant information you need quickly Live references are linked to PubMed referring you to the latest journal material Customise the contents you can highlight sections and make notes Comments can be shared with colleagues tutors for discussion teaching and learning The text can also be reflowed for ease of reading Text and illustrations copied will be automatically referenced to Kucers The Use of Antibiotics

Kucers' The Use of Antibiotics M. Lindsay Grayson, Sara E. Cosgrove, Suzanne Crowe, William Hope, James S. McCarthy, John Mills, Johan W. Mouton, David L. Paterson, 2017-10-02 Kucers The Use of Antibiotics is the definitive internationally authored reference providing everything that the infectious diseases specialist and prescriber needs to know about antimicrobials in this vast and rapidly developing field The much expanded Seventh Edition comprises 4800 pages in 3 volumes in order to cover all new and existing therapies and emerging drugs not yet fully licensed Concentrating on the treatment of infectious diseases the content is divided into four sections antibiotics anti fungal drugs anti parasitic drugs and anti viral drugs and is highly structured for ease of reference Each chapter is organized in a consistent format covering susceptibility formulations and dosing adult and pediatric pharmacokinetics and pharmacodynamics toxicity and drug distribution with detailed discussion regarding clinical uses a feature unique to this title Compiled by an expanded team of internationally renowned and respected editors with expert contributors representing

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Morrissey, Jane E. Ambler, 2002 **Current Challenges in the Treatment of Respiratory Tract Infections** John G. Bartlett, 1997 **Fluoroquinolone Antibiotics** Allan R. Ronald, Donald Low, 2003-04-01 The quinolones are making a significant contribution to patient care and have added a new dimension to antibacterial therapy During the last decade they became important agents for treating hospital acquired infections This volume covers their mechanisms of action resistance mechanisms and epidemiology pharmacokinetics safety and clinical applications Their effectiveness for respiratory urinary sexually transmitted skin soft tissue bone and joint infections infections of the eyes ears nose and throat and less common infections such as mycobacterial Brucella and others are reviewed Also described is their use in pediatric oncology and immunocompromised patients The quinolone story continues to be intriguing with exciting future implications This monograph is an important comprehensive review and update for researchers and clinicians in pharmacology clinical medicine molecular and cell biology epidemiology and the pharmaceutical industry Newer Fluoroquinolones and the Management of Respiratory Tract Infections, 2000 **Current Challenges in the Treatment of Respiratory Tract Infections**, 1997 Fluoroquinolones in the Treatment of Infectious Diseases W. Eugene Sanders, Christine C. Sanders, 1990 Microbiology of Fluoroquinolones Pharmacokinetics and Tissue Penetration of Fluoroquinolones Fluoroquinolone Therapy of Urinary Tract Infections Fluoroquinolones in Skin and Skin Structure Infections Fluoroquinolones in Bone and Joint Infections Ciprofloxacin for Respiratory Tract Infections Fluoroquinolones in Sexually Transmitted Diseases Fluoroquinolones in the Treatment of Infectious Diarrhea The Use of Fluoroquinolones in Neutropenic Patients Bronchopulmonary Infections in Cystic Fibrosis Pathophysiology and Treatment Use of fluoroquinolones in the treatment of surgically related infections Fluoroquinolones for the treatment of foot infections in patients with diabetes mellitus The use of fluoroquinolones in miscellaneous injections Adverse reactions to fluoroquinolones Pharmacoeconomic implications of oral fluoroquinolone therapy New developments in fluoroquinolone therapy *Fluoroquinolones for the Treatment of Other Respiratory Tract Infections* Tara Cowling, Kelly Farrah, 2019 Fluoroquinolones FQs are a common class of antibiotic used for the treatment of infections including those of the respiratory tract However the use of FQs has been controversial as certain types are associated with antibiotic resistance and adverse events **Community-Acquired Respiratory Infections** Charles H. Nightingale, Paul Ambrose, Thomas M. File, Jr., 2003-08-20 Up to date information The book is well supplied with references that are easily accessible Doody's Electronic Journal **Chemoprophylaxis and Virus Infections of the Respiratory Tract** J.S. Oxford, 2018-10-24 Originally it was our intention to produce a single volume book covering all aspects and approaches to the problem of specific inhibitors of respiratory viruses However as the work progressed it became obvious that certain chapters because of the research interests of the authors concentrated particularly on influenza viruses It seemed logical therefore to divide the book into two volumes the first emphasizing influenza and the second concentrating on other viruses as well as discussing important general aspects of drug screening

and clinical testing although the second volume does have some chapters which deal mainly with influenza **1st International Consensus Workshop on Fluoroquinolones in Respiratory Tract Infections, 28 February-1 March 1997, Dresden, Germany ,1998 Fluoroquinolones for the Treatment of Respiratory Tract Infections** Tara Cowling,Kelly Farrah,2019 This report aims to identify and synthesize the evidence describing the clinical effectiveness cost effectiveness and evidence based guidelines for the treatment of respiratory tract infections including pneumonia and chronic obstructive pulmonary disease COPD using Fluoroquinolones *Respiratory Infections* James Pennington,1983 Both a timely bedside guide to diagnosis and modern therapies and a reference text for the latest etiology oriented information on pathogenesis of respiratory infections In the five years since publication of the second edition new agents causing pneumonia have been described increasing drug resistance among established pathogens has occurred and there are some promising new therapeutic agents available Every chapter in this edition is therefore updated some like the chapter dealing with HIV associated respiratory diseases are almost entirely rewritten Annotation copyright by Book News Inc Portland OR

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