Contents

Preface xiii
Keith S. Kaye and Donald Kaye

Antibacterial Susceptibility Testing in the Clinical Laboratory 757
Thomas L. Holland, Christopher W. Woods, and Maria Joyce

This article familiarizes the clinician with the principles of bacterial susceptibility testing and reporting to facilitate communication with the clinical microbiology laboratory. As resistance continues to emerge among a wide range of clinically relevant bacteria, the complexity of this communication increases. This updated version provides an overview of the important susceptibility concerns for most commonly isolated bacterial pathogens.

Pharmacokinetics and Pharmacodynamics of Antibacterial Agents 791
Matthew E. Levison and Julie H. Levison

This article reviews pharmacodynamics of antibacterial drugs, which can be used to optimize treatment strategies, prevent emergence of resistance and rationalize the determination of antimicrobial susceptibility. Important pharmacodynamic concepts include the requirements for bactericidal therapy for endocarditis and meningitis, for synergistic combinations to treat enterococcal endocarditis or to shorten the course of antimicrobial therapy, for obtaining maximal plasma concentration/minimal inhibitory concentration (MIC) ratios that are greater than 10 or 24 hour-area under the plasma concentration curve (AUC)/MIC ratios that are greater than 100-125 for concentration-dependent agents against gram-negative bacilli and 25-35 against Streptococcus pneumoniae, and for obtaining percent of time that drug levels are greater than the MIC that is at least 40% to 50% of the dosing interval for time-dependent agents.

Pathogens Resistant to Antibacterial Agents 817

Resistance to antimicrobial drugs is increasing at an alarming rate among both gram-positive and gram-negative bacteria. Traditionally, bacteria resistant to multiple antimicrobial agents have been restricted to the nosocomial environment. A disturbing trend has been the recent emergence and spread of resistant pathogens in nursing homes, in the community, and in the hospital. This article reviews the epidemiology, molecular mechanisms of resistance, and treatment options for pathogens resistant to antimicrobial drugs.

Controlling Antimicrobial Resistance in the Hospital 847
Deverick J. Anderson and Keith S. Kaye

Most evidence-based methods to control the spread of antimicrobial resistance have been developed and applied to the hospital setting.
Strategies to control the emergence and spread of antimicrobial resistance in hospitals can be categorized as either infection control or antibiotic stewardship strategies. Infection control is the discipline focused on preventing the spread of infections within the health care setting; antibiotic stewardship can help minimize the emergence of multidrug-resistant organisms by promoting prudent use of antibiotics. This article describes different infection control and antibiotic management strategies that can be used to control antimicrobial resistance in hospital settings.

Antibacterial Agents in Pediatrics
Susana Chavez-Bueno and Terrence L. Stull

Antibiotics are among the most frequently used drugs in children. Although antibacterials have been available for decades, many agents have not been studied to assess their safety and efficacy in the pediatric population. This article describes the pharmacologic characteristics and therapeutic use of the most commonly prescribed antibacterials for pediatric patients. Newer agents currently under clinical investigation are discussed as well.

Antibacterial Agents in the Elderly
Stephen Weber, Emily Mawdsley, and Donald Kaye

Older patients disproportionately suffer the burden of infection in the community and in health care facilities. The rational approach to antimicrobial therapy for older patients with infection requires an appreciation and understanding of the complex immunologic, epidemiologic, pharmacologic, and microbiologic factors that influence the manifestations and consequences of infection in this group. Specific recommendations for common infectious syndromes must take into account the unique needs of older patients and should be tailored for each individual case.

Use of Antibacterial Agents in Renal Failure
Brett Gilbert, Paul Robbins, and Lawrence L. Livornese, Jr

This article provides background information on the pharmacokinetics of antibacterial agents in patients who have normal and impaired renal function. Tables are provided to allow quick determination of appropriate dosages for varying degrees of renal failure. The use of serum levels; newer strategies for cefazolin, vancomycin and aminoglycoside dosing; methods of dialysis and associated antibiotics dosage adjustments, and antibiotic toxicity in renal failure are reviewed.

Strategies and New Developments in the Management of Bacterial Meningitis
Justine Miranda and Allan R. Tunkel

The principles of antimicrobial therapy for acute bacterial meningitis include use of agents that penetrate well into cerebrospinal fluid and attain appropriate cerebrospinal fluid concentrations, are active in purulent cerebrospinal fluid, and are bactericidal against the infecting pathogen.
Recommendations for treatment of bacterial meningitis have undergone significant evolution in recent years, given the emergence of pneumococcal strains that are resistant to penicillin. Clinical experience with use of newer agents is limited to case reports, but these agents may be necessary to consider in patients who are failing standard therapy.

Topical Antibacterial Agents

Peter A. Lio and Elaine T. Kaye

Decreased systemic toxicity, ease of application, and increased concentrations at the target site are some of the important advantages topical antibacterial agents offer. This article reviews the literature on selected indications for these agents and provides in-depth examination of specific agents for the prophylaxis and treatment of skin and wound infections.

Antibiotics for Gram-Positive Bacterial Infections: Vancomycin, Teicoplanin, Quinupristin/Dalfopristin, Oxazolidinones, Daptomycin, Dalbavancin, and Telavancin

Michael D. Nailor and Jack D. Sobel

An overview of the mechanism of action, dosing, clinical indications, and toxicities of the glycopeptide vancomycin is provided. The emerging gram-positive bacterial resistance to antimicrobials and its mechanisms are reviewed. Strategies to control this emergence of resistance are expected to be proposed. Newer antimicrobial agents that have activity against vancomycin-resistant organisms are now available and play a critical role in the treatment of life-threatening infections.

Newer Beta-lactam Antibiotics: Doripenem, Ceftobiprole, Ceftaroline, and Cefepime

Jose A. Bazan, Stanley I. Martin, and Kenneth M. Kaye

This article reviews the new beta-lactam (β-lactam) antibiotics doripenem, ceftobiprole, and ceftaroline. It covers pharmacokinetic and pharmacodynamic properties, dosing, in vitro activities, safety, and clinical trial results. Doripenem (Doribax) has been approved by the US Food and Drug Administration (FDA) for the treatment of complicated intra-abdominal and urinary tract infections. At this writing, ceftobiprole is under review by the FDA for approval based on results of phase 3 clinical trials, whereas at least one phase 3 clinical trial of ceftaroline has been completed. The article also reviews recent data suggesting increased overall mortality with Cefepime (Maxipime) use compared with other beta-lactam antibiotics and the potential risk for neurotoxicity in the setting of renal failure.

Macrolides, Ketolides, and Glycylcyclines: Azithromycin, Clarithromycin, Telithromycin, Tigecycline

Jerry M. Zuckerman, Fozia Qamar, and Bartholomew R. Bono

The advanced macrolides, azithromycin and clarithromycin, and the ketolide, telithromycin, are structural analogs of erythromycin. They have
several distinct advantages when compared with erythromycin, including enhanced spectrum of activity, more favorable pharmacokinetics and pharmacodynamics, once-daily administration, and improved tolerability. Clarithromycin and azithromycin are used extensively for the treatment of respiratory tract infections, sexually transmitted diseases, and Helicobacter pylori–associated peptic ulcer disease. Telithromycin is approved for the treatment of community-acquired pneumonia. Severe hepatotoxicity has been reported with the use of telithromycin.

The Newer Fluoroquinolones
Maureen K. Bolon

Clinicians have enthusiastically used fluoroquinolones owing to their good safety profile and wide range of indications. This article reviews fluoroquinolone pharmacology, pharmacodynamic principles, and fluoroquinolone resistance mechanisms, highlighting recent trends in the epidemiology of fluoroquinolone resistance among gram-negative organisms and Streptococcus pneumoniae. Important fluoroquinolone safety concerns are discussed, along with indications for the most commonly used fluoroquinolones—ciprofloxacin, levofloxacin, and moxifloxacin.

Current Use for Old Antibacterial Agents: Polymyxins, Rifamycins, and Aminoglycosides
Luke F. Chen and Donald Kaye

This article reviews three classes of antibacterial agents that are uncommonly used in bacterial infections and therefore can be thought of as special-use agents. The polymyxins are reserved for gram-negative bacilli that are resistant to virtually all other classes of drugs. Rifampin is used therapeutically, occasionally as a companion drug in treatment of refractory gram-positive coccal infections, especially those involving foreign bodies. Rifaximin is a new rifamycin that is a strict enteric antibiotic approved for treatment of traveler's diarrhea and is showing promise as a possible agent for refractory Clostridium difficile infections. The aminoglycosides are used mainly as companion drugs for the treatment of resistant gram-negative bacillary infections and for gram-positive coccal endocarditis.