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.

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.

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.

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. Ceftaroline has received FDA approval for the treatment of skin and soft tissue infections and community acquired pneumonia. Ceftobiprole has not received FDA approval. 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.

Review of Macrolides (Azithromycin, Clarithromycin), Ketolids (Telithromycin) and Glycylcyclines (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.