caused by *H. influenzae, N. meningitidis*, and susceptible strains of *S. pneumoniae*. It is also used for the treatment of later-stage Lyme disease, gonococcal infections, and streptococcal endocarditis. It is noteworthy that ceftazidime is the only third-generation cephalosporin with activity against *Pseudomonas aeruginosa*, but it lacks activity against gram-positive bacteria. This drug is frequently used for pulmonary infections in cystic fibrosis, postneurosurgical meningitis, and febrile neutropenia. The fourth generation of cephalosporins includes cefepime and cefpirome, broad-coverage agents with potent activity against both gram-negative bacilli, including *P. aeruginosa*, and gram-positive cocci. The fourth generation has clinical applications similar to those of the third generation and may offer additional activity over the first, second, and third generations in the presence of certain β-lactamases. These agents can be used in bacteremia, febrile neutropenia, and intraabdominal and urinary tract infections. Ceftaroline, a fifth-generation cephalosporin, differs from the other cephalosporins in its added activity against MRSA, which is resistant to all other β-lactams. Ceftaroline's gram-negative activity is similar to that of the third-generation cephalosporins but does not include *P. aeruginosa*. Ceftaroline may be used in community-acquired pneumonia and skin infections, and emerging data support its use in more severe infections such as bacteremia. Adverse reactions to ceftaroline have included hypersensitivity reactions and neutropenia. Ceftolozane-tazobactam and ceftazidime-avibactam are novel cephalosporin–β-lactamase inhibitor combinations with activity against gram-negative bacteria, including *Pseudomonas*, and some anaerobes. Both agents have been studied in complicated intraabdominal infections and complicated urinary tract infections. Ceftolozane-tazobactam is thought to be stable against many ESBL-producing organisms because of the tazobactam component. The addition of avibactam to ceftazidime yields a combination agent with activity against AmpC-, ESBL-, and *K. pneumoniae* carbapenemase (KPC)–producing organisms. These cephalosporin–β-lactamase inhibitor combinations may be of clinical benefit in multidrug-resistant gram-negative infections.