Newer Fluoroquinolones and the Management of Respiratory Tract Infections

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Infections of the respiratory tract remain one of the leading causes of death in the United States [1]. The cost burden for bacterial infections of the upper and lower respiratory tract is tremendous; the cost alone of treating patients with community-acquired pneumonia (CAP) has recently been estimated to be close to $10 billion (US) [2]. In addition, the emergence of drug-resistant pathogens presents a challenge to infectious disease clinicians. Several common respiratory tract pathogens, including *Streptococcus pneumoniae* and *Haemophilus influenzae*, have shown a progressive tendency to develop resistance to both β-lactams and non-β-lactam antibiotics.

National and international multicenter surveillance programs have been tracking the prevalence and patterns of antimicrobial resistance among respiratory tract pathogens. At the local level, these surveillance programs can be used to help guide therapeutic decisions. Neuer antimicrobials for the treatment of CAP, such as the newer fluoroquinolones, offer significant advantages over existing agents, including a broader spectrum of activity, improved safety, higher bioavailability, and reduced resistance potential. These agents may also offer shorter courses of therapy, enhanced patient compliance, and potential economic savings. The newer fluoroquinolones, which have been engineered to exhibit enhanced gram-positive activity while maintaining gram-negative activity, are frequently active against resistant bacterial strains.

There are 2 means by which bacteria can become resistant to fluoroquinolones: mutations in 1 or both of fluoroquinolone enzyme targets and overexpression of multidrug efflux pumps. Each fluoroquinolone has different relative activities against the enzymes, which may also vary with the type of pathogen. Enzyme targets may be more susceptible to the newer fluoroquinolones, thereby decreasing the likelihood of bacterial resistance. Knowledge of these variations is important in selecting the appropriate dosage regimen for clinical care.

The discovery of multiple drug-resistant *S. pneumoniae* (DRSP), which is defined as having reduced susceptibility to ≥2 antibacterials, has heightened the interest in fluoroquinolones. Some formerly potent antipneumococcal agents, such as the β-

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