



Symposium 1.2

Mechanisms of Pneumococcal Resistance and Their Clinical Implications

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Over the past 2 decades, antimicrobial resistance among *Streptococcus pneumoniae*, the most common cause of community-acquired pneumonia (CAP), has escalated dramatically worldwide. By the early 1990s, penicillin-resistant clones of *S. pneumoniae* spread rapidly across Europe and globally. Additionally, resistance to macrolides and other antibiotic classes escalated in tandem with penicillin resistance. Six international clones (serotypes 6A, 6B, 9V, 14, 19F, 23F) were responsible for most of these resistant isolates. Currently, 20 to 30% of *S. pneumoniae* worldwide are multidrug resistant (MDR) (i.e. resistant to > or = 3 different classes of antibiotics). Fluoroquinolone resistance has remained stable in most countries with rates < 2%. Despite the dramatic escalation in the rate of antimicrobial resistance among pneumococci worldwide, the clinical impact of antimicrobial resistance is difficult to define. Treatment failures due to antibiotic-resistant pneumococci have been reported with meningitis, otitis media, and lower respiratory tract infections, but the relation between drug resistance and treatment failures has not been convincingly established. There is only a single report of documented microbiologic failure of parenteral penicillin-class antibiotics in the treatment of pneumococcal pneumonia in patients with or without bacteremia, however, there are numerous well-documented reports of treatment failure with quinolone-class ($n \geq 21$) and macrolide-class ($n \geq 33$) antibiotics in the treatment of pneumococcal pneumonia. As a result of these reports the new IDSA/ATS CAP guidelines have recommended that a macrolide not be used empirically when high-level macrolide resistant rates are $\geq 25\%$. However, two recent population-based studies have documented an increase in clinical failure when discordant macrolide therapy is used, including low-level resistance. It is time that guidelines are developed to help guide clinicians regarding the prevalence of resistance at which we should abandon an antibiotic class or agent within the class.