



Molecular Mechanisms of Resistance in *Streptococcus pneumoniae* : Will MICs Creep Ever Higher?

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S*treptococcus pneumoniae* is a leading cause of pneumonia, bacteremia, sepsis and meningitis with an estimated annual incidence of invasive disease of 12-17 cases per 100,000 population per year. Antimicrobial therapy has resulted in a reduction of the morbidity and mortality associated with invasive pneumococcal disease especially when administered early in the course of illness. However, the success of antimicrobial therapy is threatened by the increasing prevalence of antimicrobial resistance in *S. pneumoniae*. There is increasing evidence that discordant empiric therapy at presentation results in increased morbidity and mortality in serious bacterial infections. However, we have been able to overcome this in part by either increasing the dose of antimicrobial, i.e., penicillin, amoxicillin, or by the use of more active drugs in the class to which resistance has emerged, i.e., moxifloxacin and gemifloxacin. Unfortunately, what we are witnessing now is what appears to be MIC creep. Strains of pneumococci are appearing with;

1. increasing levels of β -lactam resistance,
2. increasingly efficient efflux pumps,
3. increasing numbers of mutations in target sites,
4. and new mechanisms of resistance which when in combination with other well recognized resistant mechanisms elevate the MIC to levels not achievable with our current antibiotics.