



### Symposium 1.3

## Treating CAP in the era of resistance

**Keith P Klugman**

Hubert Department of Global Health  
Emory University  
Atlanta, GA, USA

The principles of CAP treatment are to be found in an understanding of the principles of PK/PD as they apply to the major classes of drugs used to treat CAP and the emerging levels of resistance to these agents among treatable bacterial pathogens. Injectable betalactams active against resistant pneumococci are unlikely to fail against strains with MIC's up to 4 µg/ml. An exception is cefuroxime treatment of adults where MIC's against penicillin – resistant pneumococci are likely to exceed 16 µg/ml. Associations of increased mortality with penicillin – resistant pneumococci need to be confirmed by demonstration of failure associated with discordance of therapy. A novel approach to demonstration of failure of discordant therapy has been the analysis of positive blood cultures in patients currently receiving oral antibiotics. These data show clear evidence of an association between positive blood cultures and therapy discordance for oral macrolides i.e. macrolide resistance associated with failure of macrolide monotherapy. The distribution of macrolide failures by MIC mirrors the frequency distribution of pneumococcal isolates causing CAP in the community. Failures have thus been documented in strains with MIC's  $\geq 1$  µg/ml. It appears that higher levels of macrolide in epithelial lining fluid do not predict protection from failure of oral macrolide therapy of resistant pneumococcal CAP. Fluoroquinolone resistance seems to have plateaued in many countries at <5% probably due to the continued use of these agents only in adults. First step mutants are more common in elderly people living in long term care facilities and treatment of CAP with a fluoroquinolone should be restricted to those without previous exposure to these agents in the past 3 months. There is little call for other classes of agents in the treatment of CAP but it is of concern that linezolid resistance apparently can be selected in the pneumococcus by exposure to macrolides. Telithromycin resistance remains rare, but its empiric use in sicker patients is limited by its lesser activity against *Haemophilus influenzae*. The importance of combination therapy for pneumococcal CAP remains controversial with observational studies both supporting and refuting the hypothesis of increase efficacy of the combinations versus monotherapy.