Beta-lactams are bactericidal against intracellular forms of S. aureus in a 24-h human macrophages model (THP-1 cells)  
Maritza Barcia-Macay, Cristina Saral, Marie-Paule Mingeot-Leclercq, Paul M. Tulkens, Françoise Van Bambeke  
Pharmacologie cellulaire et moléculaire, Université catholique de Louvain - Brussels - Belgium

**Background:** Beta-lactams do not accumulate in eucaryotic cells and are usually reported as being poorly active in short-term incubation intracellular infection models. These, however, neglect the fact that beta-lactams are time-dependent antibiotics. We have examined the intracellular and extracellular activities of 4 penicillins against S. aureus over a 24-h period, using clinically-meaningful extracellular concentrations (1X MIC, 10X MIC, Cmax).

**Methods:** S. aureus ATCC 25923 (devoted of resistance mechanisms) was used throughout. Antibiotic efficacy towards extracellular (medium) and intracellular bacteria (post-phagocytosis) was determined by CFU counting.

**Results:** Extracellular and intracellular activity of Beta-lactams (S. aureus: time and concentration effects)

**Conclusion:** Despite their lack of accumulation, beta-lactams show a significant intracellular bactericidal activity. Extracellularly, all tested penicillins show a concentration-dependent bactericidal activity. Intracellularly, all penicillins were static at 3 h but slightly bactericidal at 24 h. This effect was concentration-dependent for ampicillin and oxacillin. Despite their lack of accumulation, beta-lactams show a significant intracellular activity in cells exposed to high concentrations for prolonged times, suggesting that these antibiotics have a sufficient access to the infected compartment(s).

**REFERENCES**

