

The Influence of Tissue Distribution and Protein Binding on Resistance

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Abstract

Most infections occur in the tissues of the body rather than in the blood. The site of infection is usually the extracellular compartment of tissues or body fluids such as epithelial lining fluid, bronchial secretion or middle ear fluid. Antibiotic concentrations at the site of infection may be reduced due to high protein binding or patient-related factors. The exposure of active (unbound) drug at the site of infection, where high numbers of bacteria multiply, is not only responsible for efficacy but also drives the selection pressure for resistance. To predict the propensity of antibiotic concentrations to select resistant subpopulations, pharmacokinetic and pharmacodynamic (PK/PD) parameters have been adapted. In general, higher PK/PD indices are needed to suppress resistant subpopulations than reduce the general population. The information derived from PK/PD modelling allows optimizing dosage regimens and minimizing the preferential killing of the susceptible majority, leaving a selected drug-resistant subpopulation intact. Better understanding about the influence of protein binding, PK/PD principles at tissue sites versus blood, and interaction between antibiotic treatment and commensal flora is needed to improve dosing regimens that may be less likely to promote resistance selection pressure at the site of infection.

Dr. Theuretzbacher is principal and founder of the Center for Anti-Infective Agents in Vienna, Austria, a private consulting institute dedicated to infectious diseases and anti-infective treatment. The institute provides research, education, and clinical development services to research centers, to the medical community, and to the pharmaceutical industry. In addition, Dr. Theuretzbacher lectured at the Medical University of Vienna where she designed courses in Advanced Bacteriology, Infectious Diseases and Antibiotic Treatment. A co-founder of the Medical Institute for Quality Management, Germany-Austria, Dr. Theuretzbacher organized and developed CME accredited events in the area of quality management, guideline development, and evidence based anti-infective therapy.

Dr. Theuretzbacher is secretary of the Society of Anti-Infective Pharmacology (ISAP) and manages the organizational and educational activities of the society. Additionally she is developing international scientific projects on behalf of the International Society of Chemotherapy (ISC). She has published widely read text books on clinical microbiology and authored and/or coauthored reviews, book chapters, research papers on resistance, PK/PD, and antibacterial and antifungal agent topics. Dr. Theuretzbacher is a member of the Editorial Board of the Journal Antimicrobial Agents and Chemotherapy (AAC) and reviewer for several other peer-reviewed journals.