



Antibiotic Tissue Concentration : What Really Matters

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Dose and 'traditional plasma derived' pharmacokinetic/pharmacodynamic (PK/PD) parameters (AUC/MIC, percent of time above the MIC, peak to MIC ratio) may be useful surrogates for describing response for many infection sites. This may not be the case however, when infection occurs in specialised tissue compartments, where active/restrictive transfer or efflux mechanisms exist (eg. bone, placenta, central nervous system). Since an anti-infective must come into contact with the bacterial target site for it to be effective, the optimal driver for response is the unbound concentration at the site of infection. Methods for establishing antibiotic concentrations in tissue infection sites, such as microdialysis and homogenization, may be used to obtain 'local' PK/PD links to outcome to assist in refining doses for specialised infection sites. Whether PK/PD relationships derived from tissue offer tangible advantages over those derived from plasma requires careful consideration of the infection site, the pathogen, the anti-infective, methodological limitations and the application of Occam's Razor.