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# ANTIBIOTIC THERAPY-ASSOCIATED RISKS IN CRITICALLY ILL PATIENTS

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Antibacterial therapy is a cornerstone of treatment in critically ill patients, particularly in sepsis and septic shock, where timely administration of effective antibiotics is essential for improving outcomes. However, increasing antimicrobial resistance, widespread use of broad-spectrum agents, and the complexity of intensive care populations have shifted the therapeutic challenge from simply selecting an active antibiotic toward achieving adequate antimicrobial exposure while minimizing toxicity, resistance, and ecological harm.

Critically ill patients are especially vulnerable to antibiotic-associated complications, including nephrotoxicity, hepatotoxicity, neurotoxicity, hematological adverse effects, *Clostridioides difficile* infection, clinically significant drug–drug interactions, selection of multidrug-resistant organisms, and disruption of the intestinal microbiome. These risks may be further increased by polypharmacy, prolonged antibiotic exposure, combination therapy, advanced age, and pre-existing organ dysfunction.

An important challenge is the profound and dynamic pharmacokinetic variability associated with critical illness. Capillary leak, fluid resuscitation, altered volume of distribution, hypoalbuminemia, augmented renal clearance, acute kidney injury, hepatic dysfunction, and extracorporeal organ support, including continuous renal replacement therapy (CRRT) and extracorporeal membrane oxygenation (ECMO), may substantially modify antibiotic exposure. Consequently, conventional dosing may result in either subtherapeutic concentrations, increasing the risk of treatment failure and resistance, or excessive exposure associated with toxicity.

Recent developments increasingly support a transition toward precision antimicrobial therapy. PK/PD-guided dose optimization, therapeutic drug monitoring (TDM), and model-informed precision dosing provide opportunities to individualize therapy according to rapidly changing patient characteristics. Beyond established monitoring of vancomycin and aminoglycosides, β-lactam TDM is receiving increasing attention in selected critically ill patients. Extended or

continuous β-lactam infusion may also improve PK/PD target attainment in patients with altered pharmacokinetics or less susceptible pathogens.

Modern antimicrobial stewardship is increasingly supported by rapid molecular diagnostics, earlier pathogen identification, susceptibility-guided therapy, biomarker-assisted reassessment, early de-escalation, and optimization of treatment duration. Emerging approaches integrating real-time TDM, population PK models, Bayesian forecasting, rapid diagnostics, and clinical decision-support technologies may further enable adaptive antibiotic dosing.

Thus, contemporary ICU antibiotic management should move beyond choosing the "right antibiotic" toward delivering the right drug, at the right dose and exposure, at the right time, for the right duration, with continuous reassessment of efficacy, toxicity, resistance, and ecological impact.

**Keywords:** critically ill patients, antibiotic therapy, antimicrobial resistance, precision dosing, antimicrobial stewardship.