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KEY ISSUES AND CHALLENGES IN RATIONAL ANTIBIOTIC THERAPY

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Sepsis and septic shock are life-threatening conditions in which the timely initiation of appropriate antimicrobial therapy is a critical component of effective management. At the same time, the rational selection of empirical antibiotic therapy remains a complex clinical challenge, requiring a careful balance between providing sufficiently broad initial antimicrobial coverage and minimizing the risks associated with unnecessary antibiotic exposure, drug-related toxicity, and the emergence of antimicrobial resistance.

The selection of rational empirical antibiotic therapy should consider the suspected source of infection, likely causative pathogens, local antimicrobial resistance patterns, previous antibiotic exposure, and individual risk factors for infection with multidrug-resistant organisms. Particular importance should be given to the timely collection of appropriate microbiological samples, the use of rapid diagnostic methods where available, and early reassessment of antimicrobial therapy based on microbiological and clinical findings.

Significant pharmacokinetic and pharmacodynamic alterations in critically ill patients further complicate optimal antibiotic dosing. Fluid shifts, hypoalbuminemia, impaired or augmented renal clearance, hepatic dysfunction, and the use of organ replacement therapies may substantially alter antibiotic exposure. Therefore, effective antimicrobial therapy requires individualized dosing based on PK/PD principles and, when appropriate, the use of therapeutic drug monitoring.

An essential component of rational antimicrobial management is the systematic reassessment of empirical therapy according to clinical, microbiological, and laboratory findings, followed by de-escalation, transition to targeted therapy, optimization of treatment duration, or discontinuation of antibiotics when continued therapy is no longer indicated.

Thus, contemporary empirical antibiotic therapy for sepsis should be guided not only by the principle of early treatment initiation but also by the concept of providing the right antibiotic, to the right patient, at the right dose, at the right time, and for the appropriate duration. Integrating these principles with antimicrobial stewardship represents an important strategy for improving

treatment efficacy and safety while limiting the development and spread of antimicrobial resistance.

Keywords: sepsis, septic shock, empirical antibiotic therapy, antimicrobial resistance, pharmacokinetics/pharmacodynamics, de-escalation, therapeutic drug monitoring, antimicrobial stewardship.