Chapter 3
Mechanistic Insights Into Antimicrobial Resistance: A Medical Microbiology Perspective

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ABSTRACT

Antimicrobial resistance (AMR) is considered to be one of the most significant ongoing crises in global healthcare, as it jeopardizes the effectiveness of contemporary medicine and control of infectious diseases. This chapter is a detailed review of the molecular and mechanistic pathogenesis of AMR in the context of medical microbiology. It explains the mechanisms of adaptations and survival of bacterial populations in antimicrobial pressure. Major molecular mechanisms, including enzymatic inactivation of antibiotics, alteration of target sites, overexpression of efflux pumps, and decreased membrane permeability, are thoroughly explained. The chapter goes on to discuss the resistance occurring within biofilms, and horizontal gene transfer, which provides conjugation, transformation, and transduction, is in-

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vestigated as a path of utmost importance. New alternative approaches are required to cope with this current issue. Knowledge of these molecular bases is important in creating successful antimicrobial stewardship initiatives.

1. INTRODUCTION AND CORE CONCEPTS OF ANTIMICROBIAL RESISTANCE

Antimicrobial resistance denotes the capability of microorganisms to withstand antibiotics and other antimicrobial interventions. The escalation of AMR has severely undermined the utility of many persistent antimicrobial therapies for treating infections, posing a significant obstacle to clinical care and public health. Bacterial pathogens (those causing human disease) that are impervious to available antibiotics may account for 1.27 million of the estimated 7.7 million deaths due to bacterial infections (Rush et al. 2019). Costly payment for antimicrobial resistance continues to increase. AMR is frequently presented as a single, abstract problem and, as a result, remains unseen by many stakeholders. It has evolved into a pervasive threat to the health, well-being, and prospects of most humans and other species on Earth. Today, individuals face substantial odds of encountering an antimicrobial-resistant infection at some point in life, while their ability to access effective treatment is diminishing. The health burden of resistant bacterial infections competes with or exceeds that of HIV and malaria and is a global phenomenon. AMR jeopardizes the control of infectious diseases across age groups and restricts drug development (Murray, et al. 2022). Addressing AMR requires multi-sectoral, cross-disciplinary cooperation, improved diagnostics, assessment of impacts, and effective scientific communication. Frontline defenders include clinicians, pharmacists, clinical microbiologists, and infection prevention specialists. Advances in diagnostic technology enable advanced pathogen identification and appropriate management of bloodstream infections (Peri, et al. 2024).

The threat of antimicrobial resistance is now widely regarded as the most serious hazard to human health globally. Political attention has been urged by declarations from the World Health Organization (WHO) and the U.S. Centers for Disease Control and Prevention (CDC), warning of a crisis and the prospect of reverting to a pre-antibiotic era. Patterns of antimicrobial resistance can be exploited to identify microorganisms by various phenotypic profiles (Carlet, et al. 2014). An organism resistant to at least three antibiotics representing different classes (e.g., aminoglycosides, carbapenems, cephalosporins, and/or fluoroquinolones) is classified as multidrug-resistant (MDR). Strains that remain susceptible to only one or two agents from different classes are termed extensively drug-resistant (XDR). Strains