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construction sites or to wear protective gear if this is not possible. Using a mask in encounters with high risk of aerosol transmission is recom mended. There is a general recommendation against getting new pets for the first 6–12 months after transplant. Avoiding tick and mosquito bites is particularly important. Different professional societies provide advice to transplant recipients. In the United States, the American Society of Transplantation (AST) (myast.org) and the Centers for Dis ease Control and Prevention (cdc.gov) are useful resources. Available and required immunizations vary by country, and recommendations are modified as new vaccines and new data become available. Articles published in 2023 are provided in the “Further Reading” section, but updated information may be found in the AST website, and the CDC also presents the guidelines of the Advisory Committee on Immuniza tion Practices. Specific prophylaxes against many infections have been presented in the text; a summary is presented in Table 148-3. ■ ■FURTHER READING Amengual JE, Pro B: How I treat posttransplant lymphoproliferative disorder. Blood 142:1426, 2023. Dadwal SS et al: American Society of Transplantation and Cellular Therapy Series, 2: Management and prevention of aspergillosis in hematopoietic cell transplantation recipients. Transplant Cell Ther 27:201, 2021. Fishman JA: Infection in organ transplantation. Am J Transplant 17:856, 2017. Hakki M et al: American Society for Transplantation and Cellular Therapy Series, 3: Prevention of cytomegalovirus infection and dis ease after hematopoietic cell transplantation. Transplant Cell Ther 27:707, 2021. Kaul DR et al: Ten years of donor-derived disease: A report of the dis ease transmission advisory committee. Am J Transplant 21:689, 2021. Reynolds G et al: Vaccine schedule recommendations and updates for patients with hematologic malignancy post-hematopoietic cell trans plant or CAR T-cell therapy. Transpl Infect Dis 25(suppl 1):e14109, 2023. Stewart AG, Kotton CN: What’s new: Updates on cytomegalovirus in solid organ transplantation. Transplantation 108:884, 2024. Timsit JF et al: Diagnostic and therapeutic approach to infectious diseases in solid organ transplant recipients. Intensive Care Med 45:573, 2019. Viganò M et al: Vaccination recommendations in solid organ trans plant adult candidates and recipients. Vaccines (Basel) 11:1611, 2023. Wolfe CR et al: Donor-derived guidelines: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant 33:e13547, 2019. Section 4 Therapy for Bacterial Diseases

Treatment and

Prophylaxis of Bacterial Infections David C. Hooper, Erica S. Shenoy,

Alyssa R. Letourneau, Ramy H. Elshaboury Antimicrobial agents have had a major impact on human health. Together with vaccines, they have contributed to reduced mortality, extended life span, and enhanced quality of life. Among drugs used in human medicine, however, they are distinctive in that their use

promotes the occurrence of drug resistance in the pathogens they are designed to treat as well as in other “bystander” organisms. Indeed, the history of antimicrobial development has been driven in large part by the medical need engendered by the emergence of resistance to each generation of agents. Thus, the careful and appropriate use of antimicrobial drugs is particularly important not only for optimizing efficacy and minimizing adverse effects but also for minimizing the risk of resistance and preserving the value of existing agents. Although this chapter focuses on antibacterial agents, the optimal use of all antimicro bials depends on an understanding of each drug’s mechanism of action, spectrum of activity, mechanisms of resistance, pharmacology, and adverse effect profile. This information is applied in the context of the patient’s clinical presentation, underlying conditions, and epidemiology to define the site and likely nature of the infection or other condition and thus to choose the best therapy. Gathering of microbiologic infor mation is especially important for refining therapeutic choices based on the documented pathogen and susceptibility data whenever possible; this information also makes it possible to choose more targeted therapy, thereby reducing the risk of selection of resistant bacteria that can occur with use of agents with a broader spectrum of activity than needed for the patient. Durations of therapy are chosen according to the nature of the infection and the patient’s response to treatment and are informed by clinical studies when they are available, with the understanding that shorter courses are less likely than longer courses to promote the emergence of resistance. This chapter and the one that follows provide specific information that is necessary for making informed choices among antibacterial agents. The mechanisms of action of antibacterial agents are discussed in detail in the text of this chapter, and mecha nisms of resistance are discussed in detail in Chap. 150. Both types of mechanisms, which are related to each other, are summarized for the most commonly used groups of agents in Table 150-1. A schematic of antibacterial targets is provided in Fig. 150-1.

CHAPTER 149 MECHANISMS OF ACTION

(SEE TABLE 150-1) Multiple essential components of bacterial cell structures and metabo lism have been the targets of antibacterial agents used in clinical medicine, and the interaction of an agent with its target results in either inhibition of bacterial growth and replication (bacteriostatic effect) or bacterial killing (bactericidal effect). In general, targets have been cho sen because they either do not exist in mammalian cells and physiol ogy or are sufficiently different from their mammalian counterparts to allow selective bacterial targeting. Treatment with bacteriostatic agents is effective when the patient’s host defenses are sufficient to contribute to eradication or sufficient reduction of the infecting pathogen. In patients with impaired host defenses (e.g., neutropenia) or infections at body sites with impaired or limited host defenses (e.g., meningitis and endocarditis), bactericidal agents are generally preferred. Treatment and Prophylaxis of Bacterial Infections ■ ■INHIBITION OF CELL WALL SYNTHESIS The bacterial cell wall, which is external to the cytoplasmic membrane and has no counterpart in mammalian cells, protects bacterial cells from lysis under low osmotic

conditions. The cell wall is a crosslinked peptidoglycan composed of a polymer of alternating units of N-acetylglucosamine (NAG) and N-acetylmuramic acid (NAM), four-amino-acid stem peptides linked to each NAM, and a peptide cross-bridge that links adjacent stem peptides to form a net-like structure. Several steps in peptidoglycan synthesis are targets of anti bacterial agents. Inhibition of cell-wall synthesis generally results in a bactericidal effect that is linked to cell lysis. This effect results not only from the blocking of new cell-wall formation but from the uninhibited action of cell wall–remodeling enzymes called autolysins, which cleave peptidoglycan as part of normal cell-wall growth and cell division. In gram-positive bacteria, the peptidoglycan is the most external cell structure, but in gram-negative bacteria, an asymmetric lipid outer membrane is external to the peptidoglycan and contains diffusion channels called porins. The space between the outer membrane and the peptidoglycan and cytoplasmic membrane is referred to as the periplasmic space. Most antibacterial drugs enter the gram-negative

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