CHAPTER 9

MAJOR DRUG CLASSES II

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Abstract

Major drug classes involving infectious diseases, neurological conditions, pain, and cancer represent critical therapies for acute and chronic conditions requiring specialized knowledge. Antimicrobial agents include antibacterials classified by mechanism (cell wall inhibitors, protein synthesis inhibitors, DNA/RNA disruptors) and spectrum; antivirals targeting specific viral replication steps for HIV, hepatitis, herpes, and respiratory infections; antifungals addressing superficial and systemic mycoses; and antiparasitics, with selection guided by microbial identification, susceptibility, pharmacokinetic considerations, and antimicrobial stewardship principles preventing resistance development. Central nervous system drugs include antidepressants spanning multiple mechanisms (SSRIs, SNRIs, atypical agents); antipsychotics divided into conventional and atypical classes with varying receptor profiles; mood stabilizers for bipolar disorder; anxiolytics with particular attention to dependence potential; and anticonvulsants categorized by seizure type indication and molecular targets, each requiring specific monitoring for efficacy and unique adverse effect profiles. Pain management medications range from non-opioid analgesics (acetaminophen, NSAIDs) to opioids with varying potency, duration, and formulations; adjuvant agents including anticonvulsants and antidepressants for neuropathic pain; and topical analgesics, with therapy selection balancing efficacy against adverse effects, tolerance, and abuse potential through multimodal approaches. Oncology drugs include traditional cytotoxic agents classified by mechanism (alkylating agents, antimetabolites, microtubule inhibitors); targeted therapies addressing specific molecular pathways; immunotherapies enhancing anti-tumor immune responses; hormone therapies for receptor-positive cancers; and supportive care medications managing treatment side effects, each requiring specialized handling, complex administration protocols, and comprehensive monitoring for potentially severe adverse reactions.

Keywords: *Pathogen-Specific Therapy; Neurotransmitter; Receptor Modulation; Multimodal Analgesia; Targeted Treatment; Drug Resistance*

Learning Objectives

After completion of the chapter, the learners should be able to:

- Apply antimicrobial stewardship principles to select appropriate agents based on suspected pathogens, site of infection, and local resistance patterns.
- Differentiate between the mechanisms, indications, and adverse effect profiles of various classes of central nervous system medications.
- Design multimodal pain management approaches incorporating opioid and non-opioid analgesics based on pain type, intensity, and patient-specific factors.
- Develop supportive care strategies to manage common adverse effects associated with chemotherapy and targeted cancer therapies.
- Recommend appropriate monitoring parameters for antimicrobials, CNS agents, pain medications, and oncology drugs based on efficacy and safety considerations.
- Implement risk mitigation strategies for medications with significant abuse potential or narrow therapeutic indices.

ANTIMICROBIAL AGENTS

Antimicrobial agents represent a diverse array of compounds targeting pathogenic microorganisms through various mechanisms of action. Proper selection requires consideration of the likely pathogen, infection site, patient characteristics, and local resistance patterns. The principle of antimicrobial stewardship guides judicious use to maximize therapeutic efficacy while minimizing adverse effects, resistance development, and collateral ecological damage. Pharmacists play a critical role in optimizing antimicrobial therapy through ensuring appropriate agent selection, dosing, duration, and monitoring.

Beta-Lactam Antibiotics

Beta-lactam antibiotics share a common structural element—the beta-lactam ring—and exert bactericidal effects through inhibition of cell wall synthesis. Penicillins bind to penicillin-binding proteins (PBPs), disrupting peptidoglycan cross-linking essential for bacterial cell wall integrity. Natural penicillins (penicillin G, penicillin V) demonstrate narrow-spectrum activity against gram-positive cocci and select anaerobes. Aminopenicillins (ampicillin, amoxicillin) expand coverage to include some gram-negative organisms. Antipseudomonal penicillins (piperacillin, ticarcillin) provide activity against Pseudomonas

aeruginosa and other resistant gram-negative bacilli.

Table 9.1: Antimicrobial Classes and Characteristics

Antibiotic Class	Generic Examples	Mechanism of Action	Spectrum
Penicillins	Amoxicillin Penicillin V Piperacillin	Inhibit cell wall synthesis	Gram-positive Some gram-negative
Cephalosporins - 1st Gen	Cefazolin Cephalexin	Inhibit cell wall synthesis	Gram-positive Limited gram-negative
Cephalosporins - 2nd Gen	Cefuroxime Cefaclor	Inhibit cell wall synthesis	Improved gram-negative
Cephalosporins - 3rd Gen	Ceftriaxone Cefdinir Cefpodoxime	Inhibit cell wall synthesis	Broad gram-negative Variable gram-positive
Cephalosporins - 4th/5th Gen	Cefepime Ceftaroline	Inhibit cell wall synthesis	Extended gram-negative MRSA (ceftaroline)
Carbapenems	Meropenem Ertapenem Imipenem	Inhibit cell wall synthesis	Very broad spectrum Including ESBL
Monobactams	Aztreonam	Inhibit cell wall synthesis	Aerobic gram-negative
Fluoroquinolones	Ciprofloxacin Levofloxacin Moxifloxacin	Inhibit DNA gyrase	Broad spectrum
Macrolides	Azithromycin Clarithromycin Erythromycin	Inhibit protein synthesis	Gram-positive Atypicals
Tetracyclines	Doxycycline Minocycline Tetracycline	Inhibit protein synthesis	Broad spectrum Atypicals

Antibiotic Class	Generic Examples	Mechanism of Action	Spectrum
Aminoglycosides	Gentamicin Tobramycin Amikacin	Inhibit protein synthesis	Aerobic gram-negative
Sulfonamides	Sulfamethoxazole Sulfadiazine	Inhibit folate synthesis	Variable gram-positive/negative
Oxazolidinones	Linezolid Tedizolid	Inhibit protein synthesis	Resistant gram-positive MRSA, VRE
Glycopeptides	Vancomycin Telavancin	Inhibit cell wall synthesis	Gram-positive MRSA
Lipopeptides	Daptomycin	Disrupt cell membrane	Resistant gram-positive
Antifungals - Azoles	Fluconazole Voriconazole Ketoconazole	Inhibit ergosterol synthesis	Candida Various fungi
Antifungals - Echinocandins	Caspofungin Micafungin	Inhibit cell wall synthesis	Candida Some Aspergillus
Antifungals - Polyenes	Amphotericin B Nystatin	Bind ergosterol	Broad antifungal
Antivirals - Neuraminidase Inhibitors	Oseltamivir Zanamivir	Inhibit viral release	Influenza A and B

Beta-lactamase inhibitor combinations (amoxicillin-clavulanate, piperacillin-tazobactam) overcome resistance mediated by certain bacterial enzymes that hydrolyze the beta-lactam ring. Cephalosporins, classified by generations reflecting their antimicrobial spectrum, provide increasingly broad gram-negative coverage in higher generations while often sacrificing gram-positive activity. First-generation agents (cefazolin, cephalexin) target primarily gram-positive cocci; second-generation compounds (cefuroxime, cefoxitin) offer improved gram-negative coverage; third-generation cephalosporins (ceftriaxone, cefotaxime) provide enhanced gram-negative activity including some extended-spectrum beta-lactamase (ESBL) producers;

and fourth-generation (cefepime) and fifth-generation (ceftaroline, ceftolozane) agents address specific resistance mechanisms while maintaining broad-spectrum efficacy. Carbapenems (meropenem, imipenem, ertapenem) represent the broadest-spectrum beta-lactams, reserved for multidrug-resistant infections due to their stability against most beta-lactamases. Monobactams (aztreonam) provide focused activity against aerobic gram-negative organisms without cross-reactivity in patients with penicillin allergy.

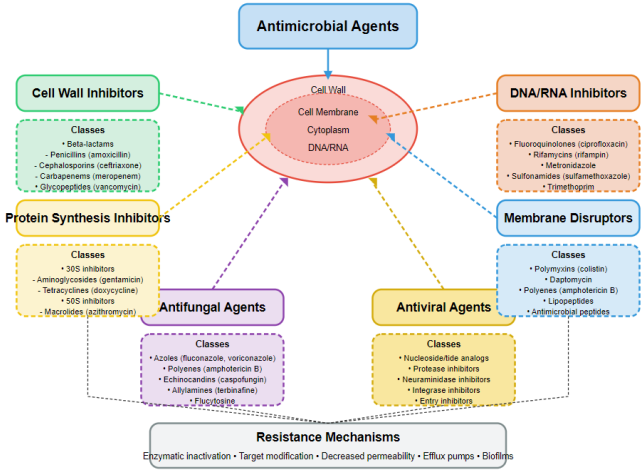

Figure 9.1: Antimicrobial Agents Classification and Mechanisms

Non-Beta-Lactam Antibiotics

Non-beta-lactam antibiotics encompass multiple structural classes with diverse mechanisms of action. Aminoglycosides (gentamicin, tobramycin, amikacin) irreversibly bind bacterial ribosomes, disrupting protein synthesis. These agents demonstrate concentration-dependent bactericidal activity against aerobic gram-negative bacilli, with enhanced efficacy through once-daily dosing regimens that maximize peak concentrations while minimizing nephrotoxicity and ototoxicity through extended drug-free intervals. Therapeutic drug monitoring guides dose optimization, particularly in patients with fluctuating renal function. Tetracyclines (doxycycline, minocycline, tigecycline) inhibit protein synthesis through reversible binding to the 30S ribosomal subunit, providing broad-spectrum activity including atypical pathogens. Newer glycylcycline derivatives overcome specific resistance mechanisms while maintaining activity against multidrug-resistant organisms. Macrolides (erythromycin, azithromycin,

clarithromycin) bind the 50S ribosomal subunit, inhibiting protein synthesis in susceptible organisms including atypical respiratory pathogens. These agents demonstrate immunomodulatory properties independent of antimicrobial effects, contributing to their utility in chronic inflammatory respiratory conditions. Quinolones, particularly fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin), inhibit bacterial DNA gyrase and topoisomerase IV, disrupting DNA replication. Their broad spectrum, excellent tissue penetration, and oral bioavailability support utility across diverse infections, though emerging safety concerns including tendinopathy, dysglycemia, and neurotoxicity have prompted more restrictive use. Oxazolidinones (linezolid, tedizolid) inhibit protein synthesis through a unique mechanism preventing formation of the initiation complex, providing activity against resistant gram-positive organisms including methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE).

Antiviral Medications

Antiviral medications target specific stages of viral replication cycles, offering therapeutic options for various viral infections. HIV treatment employs combination antiretroviral therapy (cART) incorporating multiple drug classes to suppress viral replication and prevent resistance development. Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) provide the backbone of many regimens through competitive inhibition of viral reverse transcriptase and chain termination of viral DNA synthesis. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) bind directly to reverse transcriptase, inducing conformational changes that inhibit enzymatic activity. Protease inhibitors prevent cleavage of viral polyproteins essential for production of functional viral particles. Integrase strand transfer inhibitors (INSTIs) block integration of viral DNA into the host genome, offering potent viral suppression with favorable tolerability. Entry inhibitors, including CCR5 antagonists and fusion inhibitors, prevent viral access to target cells. Hepatitis C virus (HCV) treatment has evolved dramatically with direct-acting antivirals targeting specific viral proteins including NS3/4A protease, NS5A, and NS5B polymerase, enabling interferon-free regimens with cure rates exceeding 95% across most genotypes. Influenza antivirals include neuraminidase inhibitors (oseltamivir, zanamivir) preventing viral particle release from infected cells, and polymerase inhibitors (baloxavir) disrupting viral mRNA synthesis. Herpesvirus infections utilize nucleoside analogs (acyclovir, valacyclovir, famciclovir) that undergo phosphorylation by viral thymidine kinase before inhibiting viral DNA polymerase, providing targeted activity in infected cells. Cytomegalovirus treatment employs

specialized agents (ganciclovir, valganciclovir, foscarnet) with enhanced activity against this challenging pathogen.

Antifungal and Antiparasitic Agents

Antifungal therapy addresses superficial and invasive fungal infections through targeting unique components of fungal cells. Azole antifungals (fluconazole, itraconazole, voriconazole, posaconazole) inhibit ergosterol synthesis through blocking the cytochrome P450-dependent enzyme 14-alpha-demethylase, disrupting fungal cell membrane integrity. These agents demonstrate variable spectrums of activity, with newer compounds offering enhanced coverage of molds and resistant yeasts. Significant drug interactions occur through inhibition of cytochrome P450 enzymes, necessitating careful medication reconciliation. Echinocandins (caspofungin, micafungin, anidulafungin) inhibit beta-(1,3)-D-glucan synthase, disrupting fungal cell wall synthesis. This distinct mechanism provides efficacy against resistant Candida species with favorable safety profiles due to the absence of beta-glucan in mammalian cells. Polyenes (amphotericin B) bind ergosterol directly, creating transmembrane channels that increase permeability and lead to cell death. Lipid formulations mitigate the substantial nephrotoxicity associated with conventional amphotericin B while maintaining antifungal efficacy. Antiparasitic agents address protozoal and helminthic infections through diverse mechanisms. Antimalarials include multiple classes: quinolines (chloroquine, hydroxychloroquine) preventing heme detoxification; artemisinin derivatives disrupting parasite membranes through free radical generation; and antifolates inhibiting nucleic acid synthesis. Antiprotozoal agents for intestinal and tissue infections include nitroimidazoles (metronidazole, tinidazole), quinolines, and various antiparasitic compounds with specific indications for amebiasis, giardiasis, trichomoniasis, and leishmaniasis. Antihelminthic treatment employs benzimidazoles (albendazole, mebendazole) disrupting microtubule formation, macrocyclic lactones (ivermectin) enhancing inhibitory neurotransmission, and praziquantel inducing calcium influx and paralysis in susceptible organisms.