TABLE 170-1 MECHANISMS OF ACTION OF AND RESISTANCE TO ANTIBACTERIAL AGENTS

Antibacterial Agent(s)	Major Target	Mechanism(s) of Action	Mechanism(s) of Resistance
β-Lactams (penicillins, cephalosporins, monobactams, carbapenems)	Cell wall synthesis	Bind cell wall cross-linking enzymes (PBPs, transpeptidases)	1. Drug inactivation by β-lactamases 2. Altered PBP targets 3. Reduced diffusion through porin channels
Glycopeptides (vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin)	Cell wall synthesis	Block cell wall glycosyltransferases by binding D-Ala-D-Ala stem-peptide terminus Telavancin, dalbavancin, and oritavancin: affect membrane function Oritavancin: inhibits transpeptidases	1. Altered D-Ala-D-Ala target (D-Ala-D-Lac) 2. Increased D-Ala-D-Ala target binding at sites distant from cell wall synthesis enzymes
Bacitracin	Cell wall synthesis	Blocks lipid carrier of cell wall precursors	Active drug efflux
Fosfomycin	Cell wall synthesis	Blocks linkage of stem peptide to NAG by enoyltransferase	1. Target enzyme overexpression 2. Drug-modifying enzymes
Aminoglycosides (gentamicin, tobramycin, amikacin)	Protein synthesis	Bind 30S ribosomal subunit Block translocation of peptide chain Cause misreading of mRNA	1. Drug-modifying enzymes 2. Methylation at ribosome binding site 3. Decreased permeation to target due to active efflux
Tetracyclines (tetracycline, doxycycline, minocycline)	Protein synthesis	Bind 30S ribosomal subunit Inhibit peptide elongation	1. Active drug efflux 2. Ribosomal protection proteins
Tigecycline	Protein synthesis	Same as tetracyclines	Active drug efflux (pumps different from those affecting tetracyclines)
Macrolides (erythromycin, clarithromycin, azithromycin) and ketolide (telithromycin)	Protein synthesis	Bind 50S ribosomal subunit Block peptide chain exit	1. Methylation at ribosome binding site 2. Active drug efflux
Lincosamides (clindamycin)	Protein synthesis	Bind 50S ribosomal subunit Block peptide bond formation	Methylation at ribosome binding site
Streptogramins (quinupristin, dalfopristin)	Protein synthesis	Same as macrolides	1. Same as macrolides 2. Drug-modifying enzymes
Chloramphenicol	Protein synthesis	Binds 50S ribosomal subunit Blocks aminoacyl tRNA positioning	Drug-modifying enzymes
Oxazolidinones (linezolid, tedizolid)	Protein synthesis	Bind 50S ribosomal subunit Inhibit initiation of peptide synthesis	1. Altered rRNA binding site 2. Methylation of ribosome binding site
Mupirocin	Protein synthesis	Blocks isoleucyl tRNA synthetase	1. Acquired resistant tRNA synthetase (drug bypass) 2. Altered native tRNA synthetase target
Sulfonamides (sulfadiazine, sulfisoxazole, and sulfamethoxazole)	Folate synthesis	Inhibit dihydropteroate synthetase	Acquired resistant dihydropteroate synthetase (drug bypass)
Trimethoprim	Folate synthesis	Inhibits dihydrofolate reductase	Acquired resistant dihydrofolate reductase (drug bypass)
Quinolones (norfloxacin, ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin, gemifloxacin)	DNA synthesis	Inhibit DNA gyrase and DNA topoisomerase IV Enzyme–DNA–drug complex: blocks DNA replication apparatus	1. Altered target(s) 2. Active efflux 3. Protection of target from drug 4. Drug-modifying enzyme (ciprofloxacin)
Rifamycins (rifampin, rifabutin, rifapentine)	RNA synthesis	Inhibit RNA polymerase	Altered target
Nitrofurantoin	Nucleic acid synthesis	Reduce reactive drug derivatives that damage DNA	Altered drug-activating enzymes
Metronidazole	Nucleic acid synthesis	Reduce reactive drug derivatives that damage DNA	1. Altered drug-activating enzyme 2. Acquired detoxifying enzymes 3. Active efflux
Polymyxins (polymyxin B and polymyxin E [colistin])	Cell membrane	Bind LPS and disrupt both outer and cytoplasmic membranes	Altered cell membrane charge with reduced drug binding
Daptomycin	Cell membrane	Produces membrane channel and membrane leakage	Altered cell membrane with reduced drug binding

Abbreviations: LPS, lipopolysaccharide; NAG, *N*-acetylglucosamine; PBP, penicillin-binding protein.

the only available glycylcycline, acts similarly to the tetracyclines but is distinctive for its ability to circumvent the most common mechanisms of resistance to the tetracyclines.

MACROLIDES AND KETOLIDES In contrast to the aminoglycosides and tetracyclines, the macrolides (azithromycin, clarithromycin, erythromycin) and ketolides (telithromycin) bind to the 23S rRNA of the 50S ribosomal subunit. These agents block translocation of the growing peptide chain by binding to the tunnel from which the chain exits the ribosome.

LINCOSAMIDES Clindamycin is the only lincosamide in clinical use. It binds to the 23S rRNA of the 50S ribosomal subunit, interacting with both the ribosomal A and P sites and blocking peptide bond formation.

STREPTOGRAMINS The only streptogramin in clinical use is a combination of quinupristin, a group B streptogramin, and dalfopristin, a group A streptogramin. Both components bind to 23S rRNA of the 50S ribosome: dalfopristin binds to both the A and P sites of the peptidyl transferase center, and quinupristin binds to a site that overlaps the macrolide-binding site, blocking the emergence of nascent peptide