

Bacitracin (Topical) and Fosfomycin These agents interrupt enzymatic steps in the production of peptidoglycan precursors in the cytoplasm.

■ INHIBITION OF PROTEIN SYNTHESIS

Most inhibitors of bacterial protein synthesis target bacterial ribosomes, whose difference from eukaryotic ribosomes allows selective antibacterial action. Some inhibitors bind to the 30S ribosomal subunit and others to the 50S subunit. Most protein synthesis-inhibiting agents are bacteriostatic; aminoglycosides are an exception and are bactericidal.

Aminoglycosides Aminoglycosides (amikacin, gentamicin, kanamycin, netilmicin, streptomycin, tobramycin, and plazomicin) bind irreversibly to 16S ribosomal RNA (rRNA) of the 30S ribosomal subunit, blocking the translocation of peptidyl transfer RNA (tRNA) from the A (aminoacyl) to the P (peptidyl) site and, at low concentrations, causing misreading of messenger RNA (mRNA) codons and thus causing the introduction of incorrect amino acids into the peptide chain; at higher concentrations, translocation of the peptide chain is blocked. Cellular uptake of aminoglycosides is dependent on the electrochemical gradient across the bacterial membrane. Under anaerobic conditions, this gradient is reduced, with a consequent reduction in the uptake and activity of the aminoglycosides. Spectinomycin is a related aminocyclitol antibiotic that also binds to 16S rRNA of the 30S ribosomal subunit but at a different site. This drug inhibits translocation of the growing peptide chain but does not trigger codon misreading and produces only a bacteriostatic effect.

Tetracyclines Tetracyclines (doxycycline, minocycline, tetracycline) bind reversibly to the 16S rRNA of the 30S ribosomal subunit and block the binding of aminoacyl tRNA to the ribosomal A site, thereby inhibiting peptide elongation. Active transport of tetracyclines into bacterial but not mammalian cells contributes to the selectivity of these agents. Tigecycline, a derivative of minocycline and the only available glycylcycline, acts similarly to the tetracyclines but is