anaerobic bacteria produces reactive intermediates that damage DNA and result in bactericidal activity. Both nitrofurantoin and metronidazole have selective antibacterial activity because the reducing activity needed to produce active derivatives is generated only by bacterial and not mammalian enzymes.

■ DISRUPTION OF MEMBRANE INTEGRITY

The integrity of the bacterial cytoplasmic membrane—and, in gram-negative bacteria, the outer membrane—is important for bacterial viability. Two bactericidal drugs have membrane targets.

Polymyxins The polymyxins, including polymyxin B and polymyxin E (colistin), are cationic cyclic polypeptides that disrupt the cytoplasmic membrane and the outer membrane (the latter by binding lipopolysaccharide, which is negatively charged).

Daptomycin Daptomycin is a lipopeptide that binds the cytoplasmic membrane of gram-positive bacteria in the presence of calcium, generating a channel that leads to leakage of cytoplasmic potassium ions and membrane depolarization.

PHARMACOKINETICS AND PHARMACODYNAMICS

The term *pharmacokinetics* describes the disposition of a drug in the body, whereas *pharmacodynamics* describes the drug action on the pathogen in relation to pharmacokinetic factors. An understanding of the principles governing these two areas is required for effective drug selection, dosing, and prevention of toxicities.

■ PHARMACOKINETICS

The process of drug disposition consists of four principal phases: absorption, distribution, metabolism, and excretion. These phases determine the time course of drug concentrations in serum and other tissues and body fluids.