mechanisms. Exposure to antibacterial agents either in nature or during human, animal, or other use then results in the selection of resistant strains within an otherwise susceptible bacterial population. In some cases, resistance mechanisms may confer disadvantages that render bacterial growth or survival fitness inferior to that of susceptible strains. In a number of examples, however, fitness defects are often mitigated over time by compensatory mutational mechanisms that make the bacteria both resistant and fit and thereby more likely to persist in a reservoir even in the absence of continued antimicrobial selection pressures. Discussed below are the major classes of antimicrobial agents currently in clinical use and the most important mechanisms of resistance encountered in clinical infections.

β-Lactams β-lactams, the largest class of antibiotics, inhibit bacterial cell-wall synthesis by binding to cell-wall transpeptidases, cross-linking enzymes that are also called penicillin-binding proteins (PBPs); PBPs are targets that are unique to bacteria and have no mammalian counterpart. The most common mechanism of resistance to β-lactams, particularly in gram-negative bacteria, is their degradation by β-lactamases, enzymes that break down the core β-lactam ring and destroy drug activity. β-Lactamases differ in the spectrum of β-lactams they can degrade. Some β-lactamases are encoded on the bacterial chromosome, and their activity contributes to the intrinsic susceptibility profile of a particular species. Chromosomally encoded β-lactamases can be produced in varying amounts that affect the degree of resistance. In some cases, enzyme expression is physiologically induced by exposure to certain β-lactams; in other cases, enzyme expression can become constant or constitutive through mutations in genes that encode the regulators of expression of a β-lactamase gene. Other β-lactamases are encoded by genes on acquired plasmids and are usually constitutively expressed. The resistance profiles due to plasmids may be present in some strains of a species but not others, depending on which plasmids the strain has acquired. In gram-positive bacteria β-lactamases are secreted into the extracellular environment, whereas in gram-negative bacteria these enzymes are