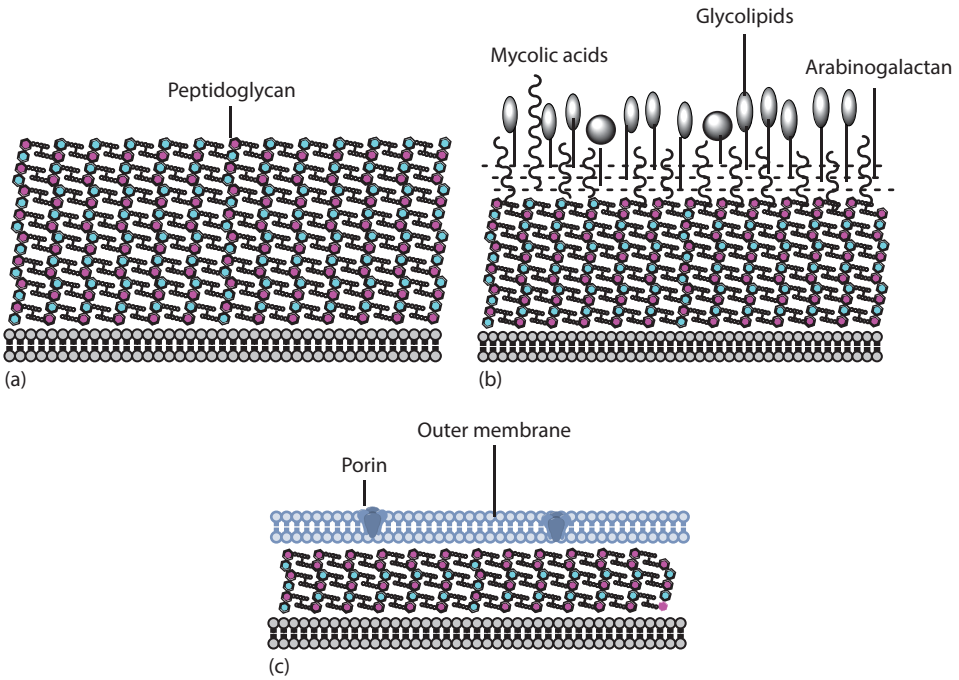

FIGURE 23.2 Schematic representation of the structure of the bacterial cell walls. (a) Gram⁺ bacteria have a thick peptidoglycan layer surrounding the plasma membrane. (c) Gram⁻ bacteria have a thin peptidoglycan layer that is surrounded by a lipid-rich bilayer outer membrane. Sandwiched between the plasma membrane and the outermembrane in Gram⁻ bacteria is a concentrated gel-like matrix (periplasm) present in periplasmic space. (b) The mycobacterial cell wall is much thicker than that of other bacteria and is hydrophobic. It consists of peptidoglycan, arabinogalactan, and mycolic acids covalently linked together to form a complex that extends from the plasma membrane outward in layers, starting with the peptidoglycan and ending with mycolic acid.

23.3.1.1 Penicillins

England and the United States made significant efforts to produce sufficient quantities of penicillin and elucidate its structure (1942–1945). Addition of corn steep liquor increased penicillin production yielding penicillin G that has a benzyl side chain. When substituted with phenoxyethanol as precursor, phenoxymethyl penicillin (penicillin V) was obtained. Penicillin V was unexpectedly acid stable and was introduced as oral penicillin. Penicillin G and V are the first-generation penicillins of narrow spectrum (Gram⁺ streptococci and staphylococci and Gram⁻ gonococci but not against Gram⁻ rods).

Preparation of other penicillins was vastly increased by the discovery of 6-aminopenicillanic acid (6-APA) which is the penicillin nucleus without any side chain attached. Batchelor et al. (1959) isolated 6-APA from fermentation media with no precursor added but the yield was very low. 6-APA could also be obtained by enzymatic removal of the side chain of penicillin by penicillin acylase (1960) or by chemical cleavage (1970).

Semisynthetic penicillins: Methicillin and oxacillin were stable to early penicillinase (an enzyme that opens the β-lactam ring and confers resistance to this class of drugs). Several derivatives followed. Amoxicillin (aminopenicillin; Table 23.1) and piperacillin (ureidopenicillin) are currently important members with improved antibacterial spectrum.

Although resistance to penicillins is widely prevalent, they continue to be the first-line antibiotics.

23.3.1.2 Cephalosporins

Brotzu discovered antibacterial activity of *Cephalosporium acremonium* (1948). Abraham et al. isolated cephalosporin P (1951), a steroid antibiotic related to fusidic acid and cephalosporin N (1954),