# Diversity among Multidrug-Resistant Enterococci

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Enterococci are associated with both community- and hospital-acquired infections. Even though they do not cause severe systemic inflammatory responses, such as septic shock, enterococci present a therapeutic challenge because of their resistance to a vast array of antimicrobial drugs, including cell-wall active agents, all commercially available aminoglycosides, penicillin and ampicillin, and vancomycin. The combination of the latter two occurs disproportionately in strains resistant to many other antimicrobial drugs. The propensity of enterococci to acquire resistance may relate to their ability to participate in various forms of conjugation, which can result in the spread of genes as part of conjugative transposons, pheromone-responsive plasmids, or broad host-range plasmids. Enterococcal hardiness likely adds to resistance by facilitating survival in the environment of a multidrug-resistant clone, thus enhancing potential spread from person to person. The combination of these attributes within the genus *Enterococcus* suggests that these bacteria and their resistance to antimicrobial drugs will continue to pose a challenge.

Enterococci, which have been known as a cause of infective endocarditis for close to a century, more recently have been recognized as a cause of nosocomial infection and "superinfection" in patients receiving antimicrobial agents (1). The enterococcus is now receiving increased attention because of its resistance to multiple antimicrobial drugs, which probably explains a large part of its prominence in nosocomial infections. The most common enterococci-associated nosocomial infections are infections of the urinary tract, followed by surgical wound infections and bacteremia (1-3). Enterococci are often present in intraabdominal and pelvic infections, although not all patients with such infections require specific antienterococcal therapy. Other enterococcal infections include infections (including meningitis and bacteremia) in very ill neonates; central nervous system infections in adults, typically with a history of central nervous system surgery or intrathecal chemotherapy; and rarely, osteomyelitis and pulmonary infections. Enterococci frequently arise from colonization of indwelling T tubes, causing liver or biliary infection in liver transplant patients (1).

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## Antimicrobial Resistance

Most enterococci have naturally occurring or inherent resistance to various drugs, including cephalosporins and the semisynthetic penicillinase-resistant penicillins (e.g., oxacillin) and clinically achievable concentrations of clindamycin and aminoglycosides. Compared with streptococci, most enterococci are relatively resistant to penicillin, ampicillin, and the ureidopenicillins, with MICs of 1 µg/ml to 8 µg/ml for most *Enterococcus faecalis* and even higher for most *E. faecium*. Many enterococci are also tolerant to the killing effects of cell-wall active agents, including ampicillin and vancomycin; recent data suggest that this property may not be inherent, but rather acquired after exposure to antibiotics (4). Inherent in vivo resistance of *E. faecalis* to trimethoprim-sulfamethoxazole may explain the lack of efficacy in animal models. In vitro, trimethoprim-sulfamethoxazole readily inhibits most enterococci at low concentrations, but this activity is lessened by exogenous folates (5). Moreover, bactericidal activity against *E. faecalis* seems unreliable and very method dependent (6). In animal models, this combination has not shown good activity and is not generally accepted