separation within *E. faecium* appears to have occurred ~3000 years ago, simultaneous with urbanization and domestication of animals. This genomic information provides new clues with regard to the evolution of enterococci from commensal organisms to important nosocomial pathogens.

EPIDEMIOLOGY

According to the National Healthcare Safety Network of the Centers for Disease Control and Prevention, enterococci are the second most common organisms (after staphylococci) isolated from hospital-associated infections in the United States. Although *E. faecalis* remains the predominant species recovered from nosocomial infections, the isolation of *E. faecium* has increased substantially in the past 20 years. In fact, *E. faecium* is now almost as common as *E. faecalis* as an etiologic agent of hospital-associated infections. This point is important, because *E. faecium* is by far the most resistant and challenging enterococcal species to treat; indeed, more than 80% of *E. faecium* isolates recovered in U.S. hospitals are resistant to vancomycin, and more than 90% are resistant to ampicillin (historically the most effective β-lactam agent against enterococci). Resistance to vancomycin and ampicillin in *E. faecalis* isolates is much less common (~7% and ~4%, respectively).

The dynamics of enterococcal transmission and dissemination in the hospital environment have been extensively studied, with a focus on vancomycin-resistant enterococci (VRE). These studies have revealed that VRE colonization of the gastrointestinal tract is a critical step in the natural history of enterococcal disease and that a substantial proportion of patients colonized with VRE remain colonized for prolonged periods (sometimes >1 year) and are more likely to develop an *Enterococcus*-related illness (e.g., bacteremia). The most important factors associated with VRE colonization and persistence in the gut include prolonged hospitalization; long courses of antibiotic therapy; hospitalization in long-term-care facilities, surgical units, and/or intensive care units; organ transplantation; renal failure (particularly in patients undergoing hemodialysis) and/or diabetes; high Acute Physiology and Chronic Health Evaluation (APACHE) scores; and physical proximity to patients infected or colonized with VRE or these patients' rooms. Once a patient becomes colonized with VRE, several key factors are involved in the organisms' dissemination in the hospital environment. VRE can survive exposure to heat and certain disinfectants and have been found on numerous inanimate objects in the hospital, including bed rails, medical equipment, doorknobs, gloves, telephones, and computer keyboards. Thus health care workers and the environment play pivotal roles in enterococcal transmission from patient to patient, and infection control measures are crucial in breaking the chain of transmission. Moreover, two meta-analyses have found that, independent of the patient's clinical status, VRE infection increases the risk of death over that among individuals infected with a glycopeptide-susceptible enterococcal strain.

The epidemiology of enterococcal disease and the emergence of VRE have followed slightly different trends in other parts of the world than in the United States. In Europe, the emergence of VRE in the mid-1980s was seen primarily in isolates recovered from animals and healthy humans rather than from hospitalized patients. The presence of VRE was associated with the use of the glycopeptide avoparcin as a growth promoter in animal feeds; this association prompted the European Union to ban the use of this compound in animal husbandry in 1996. However, after an initial decrease in the isolation of VRE from animals and humans, the prevalence of hospital-associated VRE infections has slowly increased in certain European countries, with important regional differences. For example, rates of vancomycin resistance among *E. faecium* clinical isolates in Europe are highest in Greece, the United Kingdom, and Portugal (10–30%), whereas rates in the Scandinavian countries and the Netherlands are <1%. These regional differences have been attributed in part to the implementation of aggressive "search-and-destroy" policies of infection control in countries such as the Netherlands; these policies have kept the frequency of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) and VRE very low. Despite regional differences, rates of VRE continue to be much lower in Europe than in the United States. The reasons are not totally understood, although it has been postulated that this difference is related to the higher levels of human antibiotic use in the United States. Rates of enterococcal resistance to vancomycin in some Latin American countries are also lower (~4%) than those in the United States. Conversely, in Asia, rates of vancomycin resistance among enterococci appear to be similar to those in U.S. hospitals.

As mentioned above, genomic analyses of vancomycin-resistant *E. faecium* in different parts of the world suggest that the emergence and dissemination of these organisms in the hospital environment worldwide are due to the success of a unique hospital-associated genetic clade that acquired the genes responsible for vancomycin resistance as well as other antibiotic resistance determinants.

CLINICAL SYNDROMES

URINARY TRACT INFECTION AND PROSTATITIS

Enterococci are well-known causes of nosocomial UTI—the most common infection caused by these organisms (Chap. 162). Enterococcal UTIs are usually associated with indwelling catheters, instrumentation, or anatomic abnormalities of the genitourinary tract, and it is often challenging to differentiate between true infection and colonization (particularly in patients with chronic indwelling catheters). The presence of leukocytes in the urine in conjunction with systemic manifestations (e.g., fever) or local signs and symptoms of infection with no other explanation and a positive urine culture ($\geq 10^5$ colony-forming units [CFU]/mL) suggests the diagnosis. Moreover, enterococcal UTIs often occur in critically ill patients whose comorbidities may obscure the diagnosis. In many cases, removal of the indwelling catheter may suffice to eradicate the organism without specific antimicrobial therapy. In rare circumstances, UTIs caused by enterococci may run a complicated course, with the development of pyelonephritis and perinephric abscesses that may be a portal of entry for bloodstream infections (see below). Enterococci are also known causes of chronic prostatitis, particularly in patients whose urinary tract has been manipulated surgically or endoscopically. These infections can be difficult to treat because the agents most potent against enterococci (i.e., aminopenicillins and glycopeptides) penetrate prostatic tissue poorly. Chronic prostatic infection can be a source of recurrent enterococcal bacteremia.

BACTEREMIA AND ENDOCARDITIS

Bacteremia without endocarditis is one of the most common presentations of enterococcal disease. Intravascular catheters and other devices are commonly associated with these bacteremic episodes (Chap. 168). Other well-known sources of enterococcal bacteremia include the gastrointestinal and hepatobiliary tracts; pelvic and intraabdominal foci; and, less frequently, wound infections, UTIs, and bone infections. In the United States, enterococci are ranked second (after coagulase-negative staphylococci) as etiologic agents of central line–associated bacteremia. Patients with enterococcal bacteremia usually have comorbidities and have been in the hospital for prolonged periods; they commonly have received several courses of antibiotics. Several studies indicate that the isolation of *E. faecium* from the blood may lead to worse outcomes and higher mortality rates than when other enterococcal species are isolated; this finding may be related to the higher prevalence of vancomycin and ampicillin resistance in *E. faecium* than in other enterococcal species, with the consequent reduction of therapeutic options. In many cases (usually when the gastrointestinal tract is the source), enterococcal bacteremia may be polymicrobial, with gram-negative organisms isolated at the same time. In addition, several cases have now been documented in which enterococcal bacteremia was associated with *Strongyloides stercoralis* hyperinfection syndrome in immunocompromised patients.

Enterococci are important causes of community- and health care–associated endocarditis, ranking second after staphylococci in the