close to the perineum. Hematogenously acquired osteomyelitis, especially of vertebral bodies, is more commonly caused by *E. coli* than is generally appreciated; this organism accounts for up to 10% of cases in some series (Chap. 158). *E. coli* occasionally causes orthopedic device–associated infection or septic arthritis and rarely causes hematogenous myositis. Upper-leg myositis or fasciitis due to *E. coli* should prompt an evaluation for an abdominal source with contiguous spread.

ENDOVASCULAR INFECTION Despite being one of the most common causes of bacteremia, *E. coli* rarely seeds native heart valves. When the organism does seed native valves, it usually does so in the setting of prior valvular disease. *E. coli* infections of aneurysms, the portal vein (*pylephlebitis*), and vascular grafts are quite uncommon.

MISCELLANEOUS INFECTIONS *E. coli* can cause infection in nearly every organ and anatomic site. It occasionally causes postoperative mediastinitis or complicated sinusitis and uncommonly causes endophthalmitis, ecthyma gangrenosum, or brain abscess.

BACTEREMIA *E. coli* bacteremia can arise from primary infection at any extraintestinal site. In addition, primary *E. coli* bacteremia can arise from percutaneous intravascular devices or transrectal prostate biopsy or from the increased intestinal mucosal permeability seen in neonates and in the settings of neutropenia and chemotherapy-induced mucositis, trauma, and burns. Roughly equal proportions of *E. coli* bacteremia cases originate in the community and in health care settings. In most studies, *E. coli* and *Staphylococcus aureus* are the two most common blood isolates of clinical significance. Isolation of *E. coli* from the blood is almost always clinically significant and is typically accompanied by the sepsis syndrome, severe sepsis (sepsis-induced dysfunction of at least one organ or system), or septic shock (Chap. 325).

The urinary tract is the most common source of *E. coli* bacteremia, accounting for one-half to two-thirds of episodes. Bacteremia from a urinary tract source is particularly common among patients with pyelonephritis, urinary tract obstruction, or urinary instrumentation in the presence of infected urine. The abdomen is the second most common source, accounting for 25% of episodes. Although biliary obstruction (stones, tumor) and overt bowel disruption, which typically are readily apparent, are responsible for many of these cases, some abdominal sources (e.g., abscesses) are remarkably silent clinically and require identification via imaging studies (e.g., CT). Therefore, the physician should be cautious in designating the urinary tract as the source of *E. coli* bacteremia in the absence of characteristic signs and symptoms of UTI. Soft tissue, bone, pulmonary, and intravascular catheter infections are other sources of *E. coli* bacteremia.

Diagnosis Strains of *E. coli* that cause extraintestinal infections usually grow both aerobically and anaerobically within 24 h on standard diagnostic media and are easily identified by the clinical microbiology laboratory according to routine biochemical criteria. More than 90% of ExPEC strains are rapid lactose fermenters and are indole positive.

TREATMENT EXTRAINTESTINAL *E. COLI* INFECTIONS

In the past, most *E. coli* isolates were highly susceptible to a broad range of antimicrobial agents. Unfortunately, this situation has changed. In general, the high prevalence of resistance precludes empirical use of ampicillin and amoxicillin-clavulanate, even for community-acquired infections. The prevalence of resistance to first-generation cephalosporins and TMP-SMX is increasing among community-acquired strains in the United States (with current rates of 10–40%) and is even higher outside North America. Until recently, TMP-SMX was the drug of choice for the treatment of uncomplicated cystitis in many locales. Although continued empirical use of TMP-SMX will predictably result in ever-diminishing cure rates, a wholesale switch to alternative agents (e.g., fluoroquinolones) will just as predictably accelerate the widespread emergence of resistance to these antimicrobial classes, as has already occurred in some areas. More than 90% of isolates that cause uncomplicated cystitis remain susceptible to nitrofurantoin and fosfomycin.

The prevalence of resistance to fluoroquinolones among *E. coli* isolates from U.S. outpatients has increased steadily over the last decade (i.e., from 3% in 2000 to 17.1% in 2010, according to one survey). Resistance rates are generally higher in the ambulatory setting outside the United States and are even higher in populations for which fluoroquinolone prophylaxis is used extensively (e.g., patients with leukemia, transplant recipients, and patients with cirrhosis) and among isolates from LTCFs and hospitals. For example, the National Healthcare Safety Network (NHSN) reported fluoroquinolone resistance in 41.8% of central line–associated bloodstream infection (CLABSI) *E. coli* isolates in 2009–2010, and the International Nosocomial Infection Control Consortium (INICC) reported that 53.4% of ICU *E. coli* isolates were resistant to quinolones in 2004–2009. Furthermore, the NHSN reported 19% resistance to third- and fourth-generation cephalosporins in CLABSI *E. coli* isolates, and the INICC found that 66.6% of ICU *E. coli* isolates were resistant to third-generation cephalosporins.

ESBL-producing strains are increasingly prevalent among both health care–associated (5–10%) and ambulatory isolates (region-dependent figures). An increasing number of reports describe community-acquired UTIs caused by *E. coli* strains that produce CTX-M ESBLs. Data suggest that acquisition of CTX-M-producing, fluoroquinolone-resistant strains may result from consumption of meat products from food animals treated with third- and fourth-generation cephalosporins and fluoroquinolones. Oral treatment options for such strains are limited; however, in vitro and limited clinical data indicate that, for cystitis, fosfomycin and nitrofurantoin appear to be useful options. Carbapenems and amikacin are the most predictably active agents overall, but carbapenemase-producing strains are on the rise (1–5% among health care–associated isolates in the United States and higher rates in many other countries). Tigecycline and the polymyxins, with or without a second agent, have been used most frequently against these extremely resistant isolates.

This evolving antimicrobial resistance—a source of serious concern—necessitates not only the increasing use of broad-spectrum agents but also the use of the most appropriate narrower-spectrum agent whenever possible and the avoidance of treatment of colonized but uninfected patients.

INTESTINAL PATHOGENIC STRAINS

Pathotypes Certain strains of *E. coli* are capable of causing diarrheal disease. Other important intestinal pathogens are discussed in Chaps. 160, 161, and 190–193. At least in the industrialized world, intestinal pathogenic strains of *E. coli* are rarely encountered in the fecal flora of healthy persons and instead appear to be essentially obligate pathogens. These strains have evolved a special ability to cause enteritis, enterocolitis, and colitis when ingested in sufficient quantities by a naive host. At least five distinct pathotypes of intestinal pathogenic *E. coli* exist: (1) Shiga toxin–producing *E. coli* (STEC), which includes the subsets of enterohemorrhagic *E. coli* (EHEC) and the recently evolved Shiga toxin–producing enteroaggregative *E. coli* (STEAEC); (2) enterotoxigenic *E. coli* (ETEC); (3) enteropathogenic *E. coli* (EPEC); (4) enteroinvasive *E. coli* (EIEC); and (5) enteroaggregative *E. coli* (EAEC). Diffusely adherent *E. coli* (DAEC) and cytodetaching *E. coli* are additional putative pathotypes. Lastly, a variant termed adherent invasive *E. coli* (AIEC) has been associated with Crohn's disease (although a causal role remains unproven) but does not cause acute diarrheal disease. Transmission occurs predominantly via contaminated food and water for ETEC, STEC/EHEC/STEAEC, EIEC, and EAEC and by person-to-person spread for EPEC (and occasionally STEC/EHEC/STEAEC). Gastric acidity confers some protection against infection; therefore, persons with decreased stomach acid levels are especially susceptible. Humans are the major reservoir (except for STEC/EHEC, with regard to which bovines are the main concern); host range appears to be dictated by species-specific attachment factors. Although there is some overlap, each pathotype possesses a largely unique combination of virulence traits that results in a distinctive intestinal pathogenic mechanism (Table 186-2). These strains are largely incapable of causing disease outside the