water, food, soil, and certain animals. *Citrobacter* is part of the normal fecal flora in a minority of healthy humans, but colonization rates are higher in LTCFs and hospitals—the settings in which nearly all *Citrobacter* infections occur. *Citrobacter* species account for 1–2% of nosocomial infections. The affected hosts are usually immunocompromised or have comorbid disease. *Citrobacter* causes extraintestinal infections similar to those described for other GNB.

INFECTIOUS SYNDROMES

The urinary tract accounts for 40–50% of *Citrobacter* infections. Less commonly involved sites include the biliary tree (particularly with stones or obstruction), the respiratory tract, surgical sites, soft tissue (e.g., decubitus ulcers), the peritoneum, and intravascular devices. Osteomyelitis (usually from a contiguous focus), adult central nervous system infection (from neurosurgical or other types of meningeal disruption), and myositis occur rarely. *Citrobacter* (primarily *C. koseri*) also causes 1–2% of neonatal meningitis cases, of which 50–80% are complicated by brain abscess. Further, case reports in adults suggest that *C. koseri* infection has a predilection for abscess formation. Bacteremia is most often due to UTI, biliary/abdominal infection, or intravascular device infection. *Citrobacter* occasionally causes bacteremia in neutropenic patients. Endocarditis and endovascular infections are rare.

DIAGNOSIS

Citrobacter species are readily isolated and identified; 35–50% of isolates are lactose positive, and 100% are oxidase negative. *C. freundii* is indole negative, whereas *C. koseri* is indole positive.

TREATMENT *CITROBACTER* INFECTIONS

C. freundii is more extensively resistant to antibiotics than is *C. koseri*. More than 90% of isolates are resistant to ampicillin and first- and second-generation cephalosporins. *Citrobacter* species (except *C. koseri*) possess AmpC β-lactamases; induction or selection of variants with stable derepression may develop during therapy. Resistance to antipseudomonal penicillins, aztreonam, fluoroquinolones, gentamicin, and third-generation cephalosporins is variable but increasing. The prevalence of ESBL-producing isolates is <5%. Carbapenems, amikacin, cefepime, tigecycline (with which clinical experience is limited), fosfomycin (which is available in the United States only as an oral formulation), and colistin (which is an agent of last resort because of potential toxicities) are most active, with >90% of strains susceptible.

MORGANELLA AND *PROVIDENCIA* INFECTIONS

M. morganii, *Providencia stuartii*, and (less frequently) *Providencia rettgeri* are the members of their respective genera that cause human infections. The epidemiologic associations, pathogenic properties, and clinical manifestations of these organisms resemble those of *Proteus* species. However, *Morganella* and *Providencia* occur more commonly among LTCF residents; to a lesser degree, they affect hospitalized patients. In settings with extensive use of polymyxins and tigecycline, these organisms may become increasingly common because of their intrinsic resistance to these agents.

INFECTIOUS SYNDROMES

These species are primarily urinary tract pathogens, causing UTIs that are most often associated with long-term (>30-day) catheterization. Such infections commonly lead to biofilm formation and catheter encrustation (sometimes causing catheter obstruction) or to the development of struvite bladder or renal stones (sometimes causing renal obstruction and serving as foci for relapse). *Morganella* is also commonly isolated from snakebite infection. Other, less common infectious syndromes include surgical site infection, soft tissue infection (primarily involving decubitus and diabetic ulcers), burn site infection, pneumonia (particularly ventilator-associated), intravascular device infection, and intraabdominal infection. Rarely, the other extraintestinal infections described for GNB also occur. Bacteremia is uncommon; any infected site can serve as the source, but the urinary tract accounts for most cases, with the next most common sources being surgical site, soft tissue, and hepatobiliary infections.

DIAGNOSIS

M. morganii and *Providencia* are readily isolated and identified. Nearly all isolates are lactose negative and indole positive.

TREATMENT *MORGANELLA* AND *PROVIDENCIA* INFECTIONS

Morganella and *Providencia* may be extensively resistant to antibiotics. Most isolates are resistant to ampicillin, first-generation cephalosporins, nitrofurantoin, fosfomycin, tigecycline, and the polymyxins; 40% are resistant to fluoroquinolones. *Morganella* and *Providencia* possess inducible AmpC β-lactamases; clinically significant induction or selection of stably derepressed mutants may develop during therapy. Resistance to antipseudomonal penicillins, aztreonam, gentamicin, TMP-SMX, and second- and third-generation cephalosporins is emerging but is still variably prevalent. The β-lactamase inhibitor tazobactam increases susceptibility to β-lactam agents, but sulbactam and clavulanic acid do not. Carbapenems, amikacin, and cefepime are the most active agents (>90% of isolates susceptible); however, resistance to the carbapenems, when present, is a concern because of the inherent resistance of *Morganella* and *Providencia* to the polymyxins and tigecycline. Removal of a colonized catheter or stone is critical for eradication of UTI.

EDWARDSIELLA INFECTIONS

E. tarda is the only member of the genus *Edwardsiella* that is associated with human disease. This organism is found predominantly in freshwater and marine environments and in the associated aquatic animal species. Human acquisition occurs primarily during interaction with these reservoirs and ingestion of inadequately cooked aquatic animals. *E. tarda* infection is rare in the United States; recently reported cases are mostly from Southeast Asia. This pathogen shares clinical features with *Salmonella* species (as an intestinal pathogen; Chap. 190), *Vibrio vulnificus* (as an extraintestinal pathogen; Chap. 193) and *Aeromonas hydrophila* (as both an intestinal and extraintestinal pathogen; Chap. 183e).

INFECTIOUS SYNDROMES

Gastroenteritis is the predominant infectious syndrome (50–80% of infections). Self-limiting watery diarrhea is most common, but severe colitis also occurs. The most common extraintestinal infection is wound infection due to direct inoculation, which is often associated with freshwater, marine, or snake-related injuries. Other infectious syndromes result from invasion of the gastrointestinal tract and subsequent bacteremia. Most afflicted hosts have comorbidities (e.g., hepatobiliary disease, iron overload, cancer, or diabetes mellitus). A primary bacteremic syndrome, sometimes complicated by meningitis, has a 40% case-fatality rate. Visceral (primarily hepatic) and intraperitoneal abscesses also occur. Endocarditis and empyema have been described.

DIAGNOSIS

Although *E. tarda* can readily be isolated and identified, most laboratories do not routinely seek to identify it in stool samples. Production of hydrogen sulfide is a characteristic biochemical property.

TREATMENT *EDWARDSIELLA* INFECTIONS

E. tarda is susceptible to most antimicrobial agents appropriate for use against GNB. Gastroenteritis is generally self-limiting, but treatment with a fluoroquinolone may hasten resolution. In the setting