occur with *P. vulgaris* isolates. Carbapenems, fourth-generation cephalosporins (e.g., cefepime), amikacin, TMP-SMX, and fosfomycin display excellent activity against *Proteus* species (90–100% of isolates susceptible).

ENTEROBACTER AND *CRONOBACTER* INFECTIONS

E. cloacae and *E. aerogenes* are responsible for most *Enterobacter* infections (65–75% and 15–25%, respectively); *Cronobacter sakazakii* (formerly *Enterobacter sakazakii*) and *Enterobacter gergoviae* are less commonly isolated (1% for each). *Enterobacter* species cause primarily health care–related infections. The organisms are widely prevalent in foods, environmental sources (including equipment at health care facilities), and a variety of animals. Few healthy humans are colonized, but the percentage increases significantly with LTCF residence or hospitalization. Although colonization is an important prelude to infection, direct introduction via IV lines (e.g., contaminated IV fluids or pressure monitors) also occurs. Extensive antibiotic resistance has developed in *Enterobacter* species and probably has contributed to the emergence of the organisms as prominent nosocomial pathogens. Individuals who have previously received antibiotic treatment, have comorbid disease, and are ICU residents are at greatest risk for infection. *Enterobacter* causes a spectrum of extraintestinal infections similar to that described for other GNB.

INFECTIOUS SYNDROMES

Pneumonia, UTI (particularly catheter-related), intravascular device–related infection, surgical site infection, and abdominal infection (primarily postoperative or related to devices such as biliary stents) are the most common syndromes encountered. Nosocomial sinusitis, meningitis related to neurosurgical procedures (including use of intracranial pressure monitors), osteomyelitis, and endophthalmitis after eye surgery are less frequent. *C. sakazakii* is associated with neonatal bacteremia, necrotizing enterocolitis, and meningitis (which is often complicated by brain abscess or ventriculitis); contaminated formula has been implicated as a source for such infections. *Enterobacter* bacteremia can result from infection at any anatomic site. In bacteremia of unclear origin, the contamination of IV fluids or medications, blood components or plasma derivatives, catheter-flushing fluids, pressure monitors, and dialysis equipment should be considered, particularly in an outbreak setting. *Enterobacter* can also cause bacteremia in neutropenic patients. *Enterobacter* endocarditis is rare, occurring primarily in association with illicit IV drug use or prosthetic valves.

DIAGNOSIS

Enterobacter is readily isolated and identified in the laboratory. Most strains are lactose positive and indole negative.

TREATMENT *ENTEROBACTER* INFECTIONS

Significant antimicrobial resistance exists among *Enterobacter* strains. Ampicillin and first- and second-generation cephalosporins have little or no activity. Extensive use of third-generation cephalosporins can induce or select for variants with stable derepression of AmpC β-lactamase, which confers resistance to these agents as well as monobactams (e.g., aztreonam) and—in many cases—β-lactam/β-lactamase inhibitor combinations. Resistance may emerge during therapy; in one study, this phenomenon was documented in 20% of clinical isolates. De novo resistance should be considered when clinical deterioration follows initial improvement, and third-generation cephalosporins should be avoided in the treatment of serious *Enterobacter* infections. Cefepime is stable in the presence of AmpC β-lactamases; thus, it is a suitable option for treatment of *Enterobacter* infections so long as no coexistent ESBL is present. Detection of ESBLs in *Enterobacter* is difficult because of the presence of AmpC β-lactamase; nonetheless, their prevalence (particularly in *E. cloacae*) is known to be variable worldwide but is generally increasing and is now 5–50% overall. This increase is evidenced by NHSN data, which documented resistance to third- and fourth-generation cephalosporins in 37.4% of CLABSI *Enterobacter* isolates in the United States; fortunately, carbapenems, amikacin, and tigecycline have generally retained excellent activity (90–99% susceptibility) and fluoroquinolones have good activity (85–95% susceptibility). Once susceptibility data become available, it is critical to de-escalate the antimicrobial regimen whenever possible.

SERRATIA INFECTIONS

S. marcescens causes the majority (>90%) of *Serratia* infections; *Serratia liquefaciens, Serratia rubidaea, Serratia fonticola, Serratia grimesii*, *Serratia plymuthica*, and *Serratia odorifera* are isolated occasionally. Serratiae are found primarily in the environment (including in health care institutions), particularly in moist settings. Serratiae have been isolated from a variety of animals, insects, and plants, but healthy humans are rarely colonized. In LTCFs or hospitals, reservoirs for the organisms include the hands and fingernails of health care personnel, food, milk (on neonatal units), sinks, respiratory and other medical equipment or devices, pressure monitors, IV solutions or parenteral medications (particularly those generated by compounding pharmacies), prefilled syringes and multiple-access medication vials (e.g., heparin, saline), blood products (e.g., platelets), hand soaps and lotions, irrigation solutions, and even disinfectants. Infection results from either direct inoculation (e.g., via IV fluid) or colonization (primarily of the respiratory tract). Sporadic infection is most common, but epidemics (often involving MDR strains in adult and neonatal ICUs) and common-source outbreaks also occur. The spectrum of extraintestinal infections caused by *Serratia* is similar to that for other GNB. *Serratia* species are usually considered causative agents of health care–associated infection and account for 1–3% of hospital-acquired infections. However, population-based laboratory surveillance studies in Canada and Australia demonstrated that community-acquired infections occur more commonly than was previously appreciated.

INFECTIOUS SYNDROMES

The respiratory tract, the genitourinary tract, intravascular devices, the eye (contact lens–associated keratitis and other ocular infections), surgical wounds, and the bloodstream (from contaminated infusions) are the most common sites of *Serratia* infection; the former five sites are the most common sources of *Serratia* bacteremia. Soft tissue infections (including myositis, fasciitis, mastitis), osteomyelitis, abdominal and biliary tract infection (postprocedural), and septic arthritis (primarily from intraarticular injections) occur less commonly. Serratiae are uncommon causes of neonatal or postsurgical meningitis and of bacteremia in neutropenic patients. Endocarditis is rare.

DIAGNOSIS

Serratiae are readily cultured and identified by the laboratory and are usually lactose and indole negative. Some *S. marcescens* strains and *S. rubidaea* are red pigmented.

TREATMENT *SERRATIA* INFECTIONS

Most *Serratia* strains (>80%) are resistant to ampicillin, amoxicillin-clavulanate, ampicillin-sulbactam, first-generation cephalosporins, cephamycins, nitrofurantoin, and colistin. In general, >90% of *Serratia* isolates are susceptible to other antibiotics appropriate for use against GNB. Induction or selection of variants with stable derepression of chromosomal AmpC β-lactamases may develop during therapy. Both in the United States and globally, the prevalence of ESBL-producing isolates is generally low (<5%), but rates of 20–30% have been reported in Asia and Latin America. Acquisition of carbapenemase-encoding genes is uncommon but increasing.

CITROBACTER INFECTIONS

C. freundii and *Citrobacter koseri* cause most human *Citrobacter* infections, which are epidemiologically and clinically similar to *Enterobacter* infections. *Citrobacter* species are commonly present in