monomicrobial necrotizing fasciitis; meningitis; brain, subdural, and epidural abscess; and endophthalmitis (Fig. 186-1, *middle*), particularly in the Asian Pacific Rim but also globally. Cytotoxin-producing strains of *K. oxytoca* have been implicated as a cause of hemorrhagic antibiotic-associated non–*C. difficile* colitis.

Bacteremia *Klebsiella* infection at any site can produce bacteremia. Infections of the urinary tract, respiratory tract, and abdomen (especially hepatic abscess) each account for 15–30% of episodes of *Klebsiella* bacteremia. Intravascular device–related infections account for another 5–15% of episodes, and surgical site and miscellaneous infections account for the rest. *Klebsiella* is a cause of sepsis in neonates and of bacteremia in neutropenic patients. Like enteric GNB in general, *Klebsiella* rarely causes endocarditis or endovascular infection.

DIAGNOSIS

Klebsiellae are readily isolated and identified in the laboratory. These organisms usually ferment lactose, although the subspecies *rhinoscleromatis* and *ozaenae* are nonfermenters and are indole negative. hvKP usually possesses a hypermucoviscous phenotype **(Fig. 186-1, *bottom*)**, although the sensitivity and specificity of this test are undefined and probably less than optimal. A better diagnostic test for hvKP is desirable.

TREATMENT *KLEBSIELLA* INFECTIONS

cKP and *K. oxytoca* have similar antibiotic resistance profiles. These species are intrinsically resistant to ampicillin and ticarcillin, and nitrofurantoin is inconsistently active against them. NHSN data for 2009–2010 documented resistance to third- and fourth-generation cephalosporins in 28.9% of CLABSI isolates of cKP and *K. oxytoca*, and INICC data for 2004–2009 identified resistance to third-generation cephalosporins in 76.3% of ICU isolates of *K. pneumoniae*. This increasing resistance is mediated primarily by plasmid-encoded ESBLs. In addition, such plasmids usually encode resistance to aminoglycosides, tetracyclines, and TMP-SMX. Furthermore, isolates of cKP that produce CTX-M ESBLs have been obtained from ambulatory patients with no recent health care contact (see the section on the treatment of extraintestinal *E. coli* infections for treatment considerations). Resistance to β-lactam/β-lactamase inhibitor combinations and cephamycins independent of ESBL-encoding plasmids has also been described with increasing frequency, particularly in Latin America. The prevalence of fluoroquinolone resistance is 15–20% overall and is 50% among ESBL-containing strains. Given both the undesirability of treating the latter strains with penicillins or cephalosporins and the fluoroquinolone resistance often associated with ESBLs, empirical treatment of serious or health care–associated cKP and *K. oxytoca* infections with amikacin or carbapenems is prudent, as dictated by local susceptibilities. Predictably, however, the ESBL-driven use of carbapenems has selected for strains of cKP and *K. oxytoca* that express carbapenemases. NHSN data for 2009–2010 documented resistance to carbapenems in 12.8% of CLABSI isolates of cKP and *K. oxytoca*. Treatment of infections due to strains that produce carbapenemases is highly challenging; increasingly, these strains are nearly pan-resistant. The optimal choice for therapy is unclear. Tigecycline and the polymyxins (e.g., colistin) are the most active agents in vitro and are used most frequently. However, resistance to these agents is already emerging, and strains of cKP resistant to all known antimicrobial agents have been described in the United States and globally. Combination therapy is often used in this setting.

PROTEUS INFECTIONS

Proteus mirabilis causes 90% of *Proteus* infections, which occur in the community, LTCFs, and hospitals. *Proteus vulgaris* and *Proteus penneri* are associated primarily with infections acquired in LTCFs or hospitals. *Proteus* species are part of the colonic flora of a wide variety of mammals, birds, fish, and reptiles. The ability of these GNB to generate histamine from contaminated fish has implicated them in the pathogenesis of scombroid (fish) poisoning **(Chap. 474)**. *P. mirabilis* colonizes healthy humans (prevalence, 50%), whereas *P. vulgaris* and *P. penneri* are isolated primarily from individuals with underlying disease. The urinary tract is by far the most common site of *Proteus* infection, with adhesins, flagella, IgA-IgG protease, iron acquisition systems, and urease representing the principal known urovirulence factors. *Proteus* less commonly causes infection at a variety of other extraintestinal sites.

INFECTIOUS SYNDROMES

UTI Most *Proteus* infections arise from the urinary tract. *P. mirabilis* causes only 1–2% of UTIs in healthy women, and *Proteus* species collectively cause only 5% of hospital-acquired UTIs. However, *Proteus* is responsible for 10–15% of cases of complicated UTI, primarily those associated with catheterization; indeed, among UTI isolates from chronically catheterized patients, the prevalence of *Proteus* is 20–45%. This high prevalence is due in part to bacterial production of urease, which hydrolyzes urea to ammonia and results in alkalization of the urine. Alkalization of urine, in turn, leads to precipitation of organic and inorganic compounds, which contributes to formation of struvite and carbonate-apatite crystals, formation of biofilms on catheters, and/or development of frank calculi. *Proteus* becomes associated with the stones and biofilms; thereafter, it usually can be eradicated only by removal of the stones or the catheter. Over time, staghorn calculi may form within the renal pelvis and lead to obstruction and renal failure. Thus, urine samples with unexplained alkalinity should be cultured for *Proteus*, and identification of a *Proteus* species in urine should prompt consideration of an evaluation for urolithiasis.

Other Infections *Proteus* occasionally causes pneumonia (primarily in LTCF residents or hospitalized patients), nosocomial sinusitis, intraabdominal abscesses, biliary tract infection, surgical site infection, soft tissue infection (especially decubitus and diabetic ulcers), and osteomyelitis (primarily contiguous); in rare cases, it causes nontropical myositis. In addition, *Proteus* uncommonly causes neonatal meningitis, with the umbilicus frequently implicated as the source; this disease is often complicated by development of a cerebral abscess. Otogenic brain abscess also occurs.

Bacteremia The majority of *Proteus* bacteremia episodes originate from the urinary tract; however, any of the less common sites of infection as well as intravascular devices are also potential sources. Endovascular infection is rare. *Proteus* species are occasional agents of sepsis in neonates and of bacteremia in neutropenic patients.

DIAGNOSIS

Proteus is readily isolated and identified in the laboratory. Most strains are lactose negative, produce H_2S, and demonstrate characteristic swarming motility on agar plates. *P. mirabilis* and *P. penneri* are indole negative, whereas *P. vulgaris* is indole positive. The inability to produce ornithine decarboxylase differentiates *P. penneri* from *P. mirabilis*.

TREATMENT *PROTEUS* INFECTIONS

P. mirabilis is usually susceptible to most antimicrobial agents except tetracycline, nitrofurantoin, the polymyxins, and tigecycline. Resistance to ampicillin and first-generation cephalosporins has been acquired by 10–50% of strains. Overall, 10–15% of *P. mirabilis* isolates are resistant to fluoroquinolones; 5% of isolates in the United States now produce ESBLs. Furthermore, isolates of *P. mirabilis* that produce CTX-M ESBLs have been recovered from ambulatory patients with no recent health care contact (see the section on the treatment of extraintestinal *E. coli* infections for treatment considerations). *P. vulgaris* and *P. penneri* exhibit more extensive drug resistance than does *P. mirabilis*. Resistance to ampicillin and first-generation cephalosporins is the rule, and 30–40% of isolates are resistant to fluoroquinolones. Induction or selection of variants with stable derepression of chromosomal AmpC β-lactamase may