and β-lactams; however, no studies in humans or animals support this approach at this time.

OTHER PSEUDOMONADS

STENOTROPHOMONAS MALTOPHILIA

S. maltophilia is the only potential human pathogen among a genus of ubiquitous organisms found in the rhizosphere (i.e., the soil that surrounds the roots of plants). The organism is an opportunist that is acquired from the environment but is even more limited than *P. aeruginosa* in its ability to colonize patients or cause infections. Immunocompromise is not sufficient to permit these events; rather, major perturbations of the human flora are usually necessary for the establishment of *S. maltophilia*. Accordingly, most cases of human infection occur in the setting of very broad-spectrum antibiotic therapy with agents such as advanced cephalosporins and carbapenems, which eradicate the normal flora and other pathogens. The remarkable ability of *S. maltophilia* to resist virtually all classes of antibiotics is attributable to the possession of antibiotic efflux pumps and of two β-lactamases (L1 and L2) that mediate β-lactam resistance, including that to carbapenems. It is fortunate that the virulence of *S. maltophilia* appears to be limited. Although a serine protease is present in some strains, virulence is probably a result of the host's inflammatory response to components of the organism such as LPS and flagellin. *S. maltophilia* is most commonly found in the respiratory tract of ventilated patients, where the distinction between its roles as a colonizer and as a pathogen is often difficult to make. However, *S. maltophilia* does cause pneumonia and bacteremia in such patients, and these infections have led to septic shock. Also common is central venous line–associated infection (with or without bacteremia), which has been reported most often in patients with cancer. *S. maltophilia* is a rare cause of ecthyma gangrenosum in neutropenic patients. It has been isolated from ~5% of CF patients but is not believed to be a significant pathogen in this setting.

TREATMENT *S. MALTOPHILIA* INFECTIONS

The intrinsic resistance of *S. maltophilia* to most antibiotics renders infection difficult to treat. The antibiotics to which it is most often (although not uniformly) susceptible are trimethoprim-sulfamethoxazole (TMP-SMX), ticarcillin/clavulanate, levofloxacin, and tigecycline (Table 189-2). Consequently, a combination of TMP-SMX and ticarcillin/clavulanate is recommended for initial therapy. Catheters must be removed in the treatment of bacteremia to hasten cure and prevent relapses. The treatment of VAP due to *S. maltophilia* is much more difficult than that of bacteremia, with the frequent development of resistance during therapy.

BURKHOLDERIA CEPACIA

B. cepacia gained notoriety as the cause of a rapidly fatal syndrome of respiratory distress and septicemia (the "cepacia syndrome") in CF patients. Previously, it had been recognized as an antibiotic-resistant nosocomial pathogen (then designated *P. cepacia*) in ICU patients. Patients with chronic granulomatous disease are also predisposed to *B. cepacia* lung disease. The organism has been reclassified into nine subgroups, only some of which are common in CF. *B. cepacia* is an environmental organism that inhabits moist environments and is found in the rhizosphere. This organism possesses multiple virulence factors that may play roles in disease as well as colonizing factors that are capable of binding to lung mucus—an ability that may explain the predilection of *B. cepacia* for the lungs in CF. *B. cepacia* secretes elastase and possesses components of an injectable toxin-secretion system like that of *P. aeruginosa*; its LPS is among the most potent of all LPSs in stimulating an inflammatory response in the lungs. Inflammation may be the major cause of the lung disease seen in the cepacia syndrome. The organism can penetrate epithelial surfaces by virtue of motility and inhibition of host innate immune defenses. Besides infecting the lungs in CF, *B. cepacia* appears as an airway colonizer during broad-spectrum antibiotic therapy and is a cause of VAP, catheter-associated infections, and wound infections.

TREATMENT *B. CEPACIA* INFECTIONS

B. cepacia is intrinsically resistant to many antibiotics. Therefore, treatment must be tailored according to sensitivities. TMP-SMX, meropenem, and doxycycline are the most effective agents in vitro and may be started as first-line agents (Table 189-2). Some strains are susceptible to third-generation cephalosporins and fluoroquinolones, and these agents may be used against isolates known to be susceptible. Combination therapy for serious pulmonary infection (e.g., in CF) is suggested when multidrug-resistant strains are implicated; the combination of meropenem and TMP-SMX may be antagonistic, however. Resistance to all agents used has been reported during therapy.

BURKHOLDERIA PSEUDOMALLEI

B. pseudomallei is the causative agent of melioidosis, a disease of humans and animals that is geographically restricted to Southeast Asia and northern Australia, with occasional cases in countries such as India and China. This organism may be isolated from individuals returning directly from these endemic regions and from military personnel who have served in endemic regions and then returned home after stops in Europe. Symptoms of this illness may develop only at a later date because of the organism's ability to cause latent infections. *B. pseudomallei* is found in soil and water. Humans and animals are infected by inoculation, inhalation, or ingestion; only rarely is the organism transmitted from person to person. Humans are not colonized without being infected. Among the pseudomonads, *B. pseudomallei* is perhaps the most virulent. Host compromise is not an essential prerequisite for disease, although many patients have common underlying medical diseases (e.g., diabetes or renal failure). *B. pseudomallei* is a facultative intracellular organism whose replication in PMNs and macrophages may be aided by the possession of a polysaccharide capsule. The organism also possesses elements of a type III secretion system that plays a role in its intracellular survival. During infection, there is a florid inflammatory response whose role in disease is unclear.

B. pseudomallei causes a wide spectrum of disease, ranging from asymptomatic infection to abscesses, pneumonia, and disseminated disease. It is a significant cause of fatal community-acquired pneumonia and septicemia in endemic areas, with mortality rates as high as 44% reported in Thailand. Acute pulmonary infection is the most commonly diagnosed form of melioidosis. Pneumonia may be asymptomatic (with routine chest radiographs showing mainly upper-lobe infiltrates) or may present as severe necrotizing disease. *B. pseudomallei* also causes chronic pulmonary infections with systemic manifestations that mimic those of tuberculosis, including chronic cough, fever, hemoptysis, night sweats, and cavitary lung disease. Besides pneumonia, the other principal form of *B. pseudomallei* disease is skin ulceration with associated lymphangitis and regional lymphadenopathy. Spread from the lungs or skin, which is most often documented in debilitated individuals, gives rise to septicemic forms of melioidosis that carry a high mortality rate.

TREATMENT *B. PSEUDOMALLEI* INFECTIONS

B. pseudomallei is susceptible to advanced penicillins and cephalosporins and to carbapenems (Table 189-2). Treatment is divided into two stages: an intensive 2-week phase of therapy with ceftazidime or a carbapenem followed by at least 12 weeks of oral TMP-SMX to eradicate the organism and prevent relapse. The recognition of this bacterium as a potential agent of biologic warfare has stimulated interest in the development of a vaccine.