Chronic *P. aeruginosa* Infections Chronic infection due to *P. aeruginosa* occurs mainly in the lungs in the setting of structural pulmonary diseases. The classic example is CF; others include bronchiectasis and chronic relapsing panbronchiolitis, a disease seen in Japan and some Pacific Islands. Hallmarks of these illnesses are altered mucociliary clearance leading to mucus stasis and mucus accumulation in the lungs. There is probably a common factor that selects for *P. aeruginosa* colonization in these lung diseases—perhaps the adhesiveness of *P. aeruginosa* for mucus, a phenomenon that is not noted for most other common gram-negative bacteria, and/or the ability of *P. aeruginosa* to evade host defenses in mucus. Furthermore, *P. aeruginosa* seems to evolve in ways that allow its prolonged survival in the lung without an early fatal outcome for the host. The strains found in CF patients exhibit minimal production of virulence factors. Some strains even lose the ability to produce pili and flagella, and most become complement-sensitive because of the loss of the O side chain of their LPS molecules. An example of the impact of these changes is found in the organism's discontinuation of the production of flagellin (probably its most strongly proinflammatory molecule) when it encounters purulent mucus. This response probably dampens the host's response, allowing the organism to survive in mucus. *P. aeruginosa* is also believed to lose the ability to secrete many of its injectable toxins during growth in mucus. Although the alginate coat is thought to play a role in the organism's survival, alginate is not essential, as nonmucoid strains may also predominate for long periods. In short, virulence in chronic infections may be mediated by the chronic but attenuated host inflammatory response, which injures the lungs over decades.

CLINICAL MANIFESTATIONS

P. aeruginosa causes infections at almost all sites in the body but shows a rather strong predilection for the lungs. The infections encountered most commonly in hospitalized patients are described below.

Bacteremia Crude mortality rates exceeding 50% have been reported among patients with *P. aeruginosa* bacteremia. Consequently, this clinical entity has been much feared, and its management has been attempted with the use of multiple antibiotics. Recent publications report attributable mortality rates of 28–44%, with the precise figure depending on the adequacy of treatment and the seriousness of the underlying disease. In the past, the patient with *P. aeruginosa* bacteremia classically was neutropenic or had a burn injury. Today, however, a minority of such patients have bacteremic *P. aeruginosa* infections. Rather, *P. aeruginosa* bacteremia is seen most often in patients in ICUs.

The clinical presentation of *P. aeruginosa* bacteremia rarely differs from that of sepsis in general (Chap. 324). Patients are usually febrile, but those who are most severely ill may be in shock or even hypothermic. The only point differentiating this entity from gram-negative sepsis of other causes may be the distinctive skin lesions (ecthyma gangrenosum) of *Pseudomonas* infection, which occur almost exclusively in markedly neutropenic patients and patients with AIDS. These small or large, painful, reddish, maculopapular lesions have a geographic margin; they are initially pink, then darken to purple, and finally become black and necrotic (Fig. 189-1). Histopathologic studies indicate that the lesions are due to vascular invasion and are teeming with bacteria. Although similar lesions may occur in aspergillosis and mucormycosis, their presence suggests *P. aeruginosa* bacteremia as the most likely diagnosis.

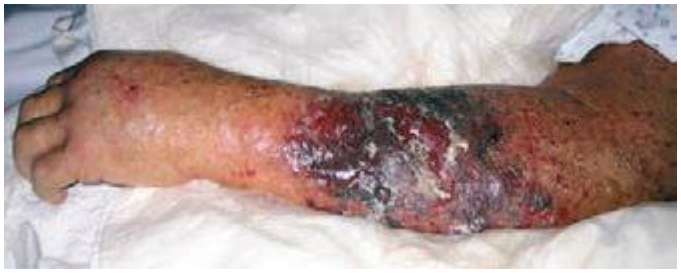

FIGURE 189-1 **Ecthyma gangrenosum** in a neutropenic patient 3 days after onset.

TREATMENT *P. AERUGINOSA* BACTEREMIA

(Table 189-2) Antimicrobial treatment of *P. aeruginosa* bacteremia has been controversial. Before 1971, the outcome of *Pseudomonas* bacteremia in febrile neutropenic patients treated with the available agents—gentamicin and the polymyxins—was dismal. However, treatment with carbenicillin, with or without an aminoglycoside, significantly improved outcomes. Concurrently, several retrospective analyses suggested that the use of two agents that were synergistic against gram-negative pathogens in vitro resulted in better outcomes in neutropenic patients. Thus, combination therapy became the standard of care—first for *P. aeruginosa* bacteremia in febrile neutropenic patients and then for all *P. aeruginosa* infections in neutropenic or nonneutropenic patients.

With the introduction of newer antipseudomonal drugs, a number of studies have revisited the choice between combination treatment and monotherapy for *Pseudomonas* bacteremia. Although the majority of experts still favor combination therapy, most of these observational studies indicate that a single modern antipseudomonal β-lactam agent to which the isolate is sensitive is as efficacious as a combination. Even in patients at greatest risk of early death from *P. aeruginosa* bacteremia (i.e., those with fever and neutropenia), empirical antipseudomonal monotherapy is deemed to be as efficacious as empirical combination therapy by the practice guidelines of the Infectious Diseases Society of America. One firm conclusion is that monotherapy with an aminoglycoside is not optimal.

There are, of course, institutions and countries where rates of susceptibility of *P. aeruginosa* to first-line antibiotics are <80%. Thus, when a septic patient with a high probability of *P. aeruginosa* infection is encountered in such settings, empirical combination therapy should be administered until the pathogen is identified and susceptibility data become available. Thereafter, whether one or two agents should be continued remains a matter of individual preference. Recent studies suggest that extended infusions of β-lactams such as cefepime or piperacillin-tazobactam may result in better outcomes of *Pseudomonas* bacteremia and possibly *Pseudomonas* pneumonia.

Acute Pneumonia Respiratory infections are the most common of all infections caused by *P. aeruginosa*. This organism appears first or second among the causes of ventilator-associated pneumonia (VAP). However, much debate centers on the actual role of *P. aeruginosa* in VAP. Many of the relevant data are based on cultures of sputum or endotracheal tube aspirates and may represent nonpathogenic colonization of the tracheobronchial tree, biofilms on the endotracheal tube, or simple tracheobronchitis.

Older reports of *P. aeruginosa* pneumonia described patients with an acute clinical syndrome of fever, chills, cough, and necrotizing pneumonia indistinguishable from other gram-negative bacterial pneumonias. The traditional accounts described a fulminant infection. Chest radiographs demonstrated bilateral pneumonia, often with nodular densities with or without cavities. This picture is now remarkably rare. Today, the typical patient is on a ventilator, has a slowly progressive infiltrate, and has been colonized with *P. aeruginosa* for days. While some cases may progress rapidly over 48–72 h, they are the exceptions. Nodular densities are not commonly seen. However, infiltrates may go on to necrosis. Necrotizing pneumonia has also been seen in the community (e.g., after inhalation of hot-tub water contaminated with *P. aeruginosa*). The typical patient has fever, leukocytosis, and purulent sputum, and the chest radiograph shows a new infiltrate or the expansion of a preexisting infiltrate. Chest examination generally detects rales or dullness. Of course, such findings are quite common among ventilated patients in the ICU. A sputum Gram's stain showing mainly polymorphonuclear leukocytes (PMNs) in conjunction with a culture positive for *P. aeruginosa* in this setting suggests a diagnosis of acute *P. aeruginosa* pneumonia. There is no consensus about whether