pathway components (C5 to C9) develop recurrent infections with *N. meningitidis* and *Neisseria gonorrhoeae.*

Although this chapter focuses on systemic immune deficiencies, it is important to consider local processes that increase the risk of focal infections in certain hosts. For example, the cystic fibrosis or chronic obstructive pulmonary disease patient with multiple bouts of pneumonia may develop localized bronchiectasis, in which normal mucociliary clearance mechanisms are inadequate to control and prevent infection. These areas are prone to recurrent bacterial infections, particularly with *Pseudomonas*. Similarly, the patient with lymphedema of a limb lacks the benefit of lymphatic drainage of early infections and is predisposed to recurrent cellulitis of the affected extremity.

PATHOLOGY

Infections in the immunocompromised host are often caused by organisms of low virulence that are able to cause infection due to impaired or absent normal defense mechanisms. Diagnosis of infection may be hampered by the small number of organisms required to cause disease and by the lack of inflammation associated with immunosuppressive conditions and therapies.

CLINICAL PRESENTATION

The clinical presentation of immunocompromised hosts with infection may be different from that seen in the immunocompetent patient. In the transplant population, typical signs and symptoms of infection such as fever, erythema, and leukocytosis may be absent as a result of the effect of immunosuppressive medications. Infections that are normally limited in scope may become disseminated in the immunocompromised host. For example, pyelonephritis involving the renal allograft may be complicated by bacteremia and acute kidney injury, both of which are uncommon in normal hosts.

Assessing the immunocompromised host with possible infection involves performing a detailed physical examination, including close inspection of the oral and periodontal tissues, perianal area, and skin. Even minor changes (e.g., faint erythematous rash, gum line erythema) may point to the source of a fever. Symptoms and signs of infection such as fever may not exist. On review of systems, subtle findings such as chills and sweats may be the only sign of an opportunistic infection. A classic finding is perianal or rectal pain without swelling or erythema, indicating a perirectal abscess in neutropenic patients. Laboratory clues to infection such as leukocytosis in the patient with systemic bacterial infection or eosinophilia in the patient with disseminated *Strongyloides* infection may be absent as a result of immunosuppressive therapy.

In many cases, the initial presentation of congenital or acquired immune deficiency states is the development of unusual or recurrent infections, and recognition of the immune defects associated with the infections can guide the diagnostic work-up. For example, the nonimmunosuppressed patient with *P. jirovecii* infection should undergo investigation for T-cell immune defects, most importantly HIV infection. The patient with recurrent *N. meningitidis* infections should be tested for possible late component complement deficiencies. Details on the manifestations of infection with the pathogens listed in Table 102-2 are found elsewhere in this textbook.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Diagnosis of infection in the immunocompromised host can be more difficult than in the normal host, and the differential diagnosis of infections can be quite broad. Because defects in humoral and cell-mediated immunity may limit the ability to develop antibody responses to infection, serologic tests have poor sensitivity for these patients. Cultures—including standard bacterial cultures and those facilitating growth of acid-fast bacilli and fungi—are often critical to making a diagnosis of infection. Because some of the pathogens causing infection in these settings are commensals or colonizers, interpretation of a positive culture result may be difficult. For example, the growth of *Candida* species in bronchoscopy specimens most likely reflects upper airway and pharyngeal colonization.

Sensitive assays to detect the DNA or RNA of opportunistic viruses—most commonly through quantitative polymerase chain reaction (PCR)—have become crucial diagnostic tests for infections such as CMV, human herpesvirus 6 (HHV-6), and BK virus, and they may help to guide the duration of antiviral therapy. Biologic markers of fungal infection such as serum galactomannan and β-D-glucan assays may suggest a diagnosis of invasive infection with molds such as *Aspergillus*.

In many cases, the diagnosis of infection may be elusive, requiring biopsy and histopathologic examination of involved tissues to determine the underlying pathogen. This process combined with tissue cultures may be needed to make a definitive diagnosis of infection in the immunocompromised host, and it can help differentiate colonization from infection with a particular organism. Biopsy of skin lesions, bone marrow, or liver may provide a diagnosis when cultures and other standard tests are unrevealing.

In neutropenic patients with fever, the procalcitonin level may be elevated in the setting of bacteremia, but it is normal in patients with fungal infections. 18-Fluorodeoxyglucose positron-emission tomography/computed tomography can help localize infection in the immunocompromised patient, in whom the sensitivity of nuclear medicine studies with indium-111, technetium-99m, or gallium may be limited.

TREATMENT AND PREVENTION OF INFECTIONS

Treatment of infections in the immunocompromised host requires rapid diagnosis and, when possible, improvement of the underlying immune disorder to help reconstitute natural immune function. In many cases, treatment must be broad spectrum and empirical while awaiting results of diagnostic testing. Delay of therapy for these patients is associated with a higher risk of dissemination and death. Details on the specific treatment recommendations for individual pathogens are found elsewhere in this textbook.

Neutropenia

For patients with neutropenic fever, empirical therapy should always include coverage for *Pseudomonas aeruginosa* because it is associated with a high mortality rate. Empirical therapy should also be guided by the individual patient's antimicrobial administration history, prior infections, colonization status (e.g., methicillin-resistant S. aureus [MRSA], vancomycin-resistant