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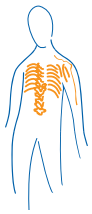
Infections in the Immunocompromised Host



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INTRODUCTION

With the development of increasingly complex and potent treatments for autoimmune, malignant, and chronic end-organ diseases, the spectrum of opportunistic infections continues to grow. Infections are the primary complication of many conditions causing immune deficiency, from congenital syndromes manifesting early in life to malignancy occurring in the elderly (Table 102-1). Success in challenging fields such as transplantation depends on preventing, quickly diagnosing, and effectively treating infections.

DEFINITION AND EPIDEMIOLOGY

The approach to the immunocompromised patient with possible infection should begin with an assessment of the arms of the immune system affected by the patient's underlying diseases and treatments.

Neutropenia

Neutropenia is a combined absolute neutrophil and band count of less than 500 cells/mm^3. It is common after chemotherapy and may be prolonged in patients with hematologic malignancies and after hematopoietic stem cell transplantation (HSCT) (see Table 102-1). In these settings, patients may develop infections from their own microbial flora or from ubiquitous environmental organisms (Table 102-2). Because some chemotherapy agents cause mucositis and other breaches of protective barriers, bacterial infections predominate in this setting, most commonly as oral mucosal, skin, soft tissue, and sinopulmonary infections. Intravenous catheter-related infections and translocation of bacteria from the gastrointestinal tract may also occur. Because *Pseudomonas* species are associated with the highest mortality rate in this setting, empirical therapy for fever in the neutropenic patient should always include antibacterial therapy to cover this organism.

Neutropenic patients are at risk for invasive fungal infection, particularly in the setting of prolonged neutropenia. *Candida* species infections are common. Sinopulmonary infections caused by *Aspergillus* and the molds of the Mucorales order are associated with considerable morbidity and mortality.

Nonchemotherapy drugs may also cause neutropenia, with a less predictable risk of infection. Responsible agents include β-lactam antibiotics, carbapenems, amphotericin B, antipsychotics, antiepileptics (e.g., carbamazepine, valproic acid, phenytoin), hydralazine, sulfonamides, and nonsteroidal anti-inflammatory agents.

The risk of infection in patients with neutropenia is inversely related to their absolute neutrophil count (i.e., neutrophils plus bands); the lower the neutrophil count and the more prolonged the period of neutropenia, the higher the risk of infection. Because chemotherapeutic agents attack native cells with rapid turnover rates, mucosae in the oropharyngeal and gastrointestinal tracts are frequently interrupted, allowing commensal and colonizing bacteria (e.g., viridans streptococci, *Escherichia coli, Klebsiella, Enterococcus, Pseudomonas*), viruses (most commonly herpes simplex virus), and fungi (especially *Candida*) to escape and replicate. In patients on prophylactic antimicrobials while neutropenic, resistant organisms can break through, resulting in bloodstream infections and sepsis with multidrug-resistant organisms.

Cell-Mediated Immunity Defects

Cell-mediated immunity defects may result from infection with certain viruses (notably human immunodeficiency virus [HIV], hepatitis C virus, and cytomegalovirus [CMV]) or from immunosuppressive agents routinely used in solid organ transplantation and in the prophylaxis and treatment of graft-versus-host disease (GVHD) in allogeneic HSCT recipients (see Table 102-1). Cell-mediated immunity defects complicate T-cell lymphoma and primary immunosuppressive conditions such as common variable immune deficiency disease (CVID). CVID, the most common primary immunodeficiency, manifests with recurrent bacterial infections (notably pneumonia and bronchitis), usually between the ages of 20 and 50 years. Patients with T-cell dysfunction or deficiency are at risk for opportunistic infections such as *Listeria monocytogenes*, CMV, *Pneumocystis jirovecii*, and invasive fungal infections (see Table 102-2).

L. monocytogenes is the most common cause of bacterial meningitis in transplant recipients. CMV causes latent infection in T cells, and the seropositive patient with late-stage HIV infection or a transplant may reactivate CMV, causing viremia or focal infection of the gastrointestinal tract, liver, lungs, or retina. Seronegative recipients of seropositive organs are at high risk for developing donor-transmitted CMV infection, which can result in long-term allograft dysfunction in addition to symptomatic infection.

P. jirovecii, a fungal pathogen, causes hypoxemia and interstitial pulmonary infiltrates in those with advanced HIV infection or T-cell dysfunction from transplantation or GVHD. Reactivation, acquisition, or donor-derived transmission of endemic fungal infections, including *Blastomyces, Coccidioides,* and *Histoplasma,* can occur. Environmental fungi, including *Aspergillus*, Mucorales