



Enterococcus [VRE]), and local susceptibility data. Broad-spectrum agents such as piperacillin-tazobactam and cefepime may be used. Carbapenems may be indicated in the patient with recent hospitalization, recent broad-spectrum antibacterial administration, or with a history of infection with extended-spectrum β -lactamase-producing Enterobacteriaceae. After a pathogen is identified in cultures and susceptibility data are available, antimicrobial therapy should be narrowed.

If a neutropenic patient remains febrile for 3 to 5 days without an identified locus or pathogen of infection, empirical glycopeptide therapy (e.g., vancomycin to cover *S. aureus*, particularly in the setting of an indwelling central catheter) and antifungal therapy are recommended to cover staphylococci and *Aspergillus* and other fungi common in this setting. Although amphotericin B products have been a mainstay of therapy for many years, voriconazole is the preferred agent to treat suspected aspergillosis because of its better efficacy in the neutropenic host.

Reconstitution of immune function in the patient with neutrophil deficiency or dysfunction can help prevent or treat infection. Administration of granulocyte colony-stimulating factor (G-CSF) (i.e., filgrastim or pegfilgrastim) with chemotherapy for solid tumors can prevent and treat absolute neutropenia and therefore reduce the risk of infection. For patients with drug-induced neutropenia, similar benefit can be attained. G-CSF usually is contraindicated in patients with myeloid malignancies and myelodysplasia due to the potential for stimulation of growth of dysplastic or malignant cells.

Several measures can help decrease the risk of infection in patients with neutropenia, including prevention of exposure to potential pathogens and antimicrobial prophylaxis. Periodontal care with oral rinses with sterile water or saline four to six times per day and gentle teeth brushing may help prevent periodontal infection and streptococcal bacteremia. Daily chlorhexidine bathing may decrease colonization with multidrug-resistant organisms that can be acquired while hospitalized. Ingestion of a low-microbial diet (e.g., no raw fruits or vegetables) and avoidance of dried or fresh flowers and potted plants may decrease exposure to fungi, including *Aspergillus*.

Housing in high-efficiency particulate air (HEPA)-filtered rooms with positive air pressure and adequate ventilation is the standard of care in HSCT units to decrease the risk of exposure to airborne pathogens. For patients at home, avoiding construction areas (including home renovation projects) while neutropenic may decrease the risk of invasive fungal infection. Patients visiting medical offices or hospitals should wear a mask, including when ambulating in the hallways or being transported for testing. Strict handwashing and hand hygiene are paramount to preventing infection. Avoidance of rectal thermometers, suppositories, enemas, and tampons while neutropenic has been recommended to prevent infection. Patients with well water should use filters to decrease the risk of *Cryptosporidium* infection. Minimization of mucositis with newer chemotherapeutic agents can help decrease the risk of infection in patients with malignancy.

Solid data support the use of quinolones (e.g., ciprofloxacin, levofloxacin) as prophylaxis for serious infection in patients with anticipated neutropenia for 7 or more days. Penicillin is often added to prevent infection with viridans streptococci in

patients on a mucositis-inducing chemotherapy regimen. Antifungal prophylaxis with voriconazole or posaconazole decreases the incidence of invasive fungal infections in patients undergoing HSCT and those with hematologic malignancies undergoing induction chemotherapy. Certain cancer patients, including those with acute lymphoblastic leukemia or those on high-dose corticosteroids, methotrexate, fludarabine, bleomycin, l-asparaginase, or cytarabine, have sufficient T-cell dysfunction to warrant prophylaxis against *P. jirovecii* (discussed later). Herpes simplex virus (HSV) prophylaxis with acyclovir is indicated for those with a history of symptomatic HSV infection or seropositivity.

Humoral Immunity Defects

Patients with hypogammaglobulinemia and CVID are at risk for infection with encapsulated organisms such as *S. pneumoniae*. Replacement of immunoglobulin G (IgG) with intravenous immune globulin (IVIG) at a dose of 400 to 600 mg/kg monthly can help prevent infections in these patients. Immunization may not be protective against *S. pneumoniae*, *H. influenzae*, or *N. meningitidis* due to poor seroconversion rates.

Hematopoietic Stem Cell Transplantation

Infection risk after HSCT depends on the source of stem cells, the type of conditioning chemotherapy regimen administered, and the risk and degree of GVHD (Fig. 102-1). Myeloablative regimens (including chemotherapy and total body irradiation) often result in severe mucositis, putting patients at risk for the infections detailed previously. Although the risk of infection in autologous transplants is relatively low due to earlier engraftment, recipients of matched unrelated donor allogeneic

Pre-engraftment Period (day 0 – day 30)

Neutropenia	}	Gram-negative bacilli (including <i>Pseudomonas</i>)
Breaks in cutaneous and mucosal barriers (e.g., IV catheters, mucositis and cystitis caused by chemotherapy)		Gram-positive cocci (<i>Staphylococcus</i> , <i>Streptococcus</i> , <i>Enterococcus</i>)
		<i>Candida</i> species
		<i>Aspergillus</i> and other invasive molds
		HSV
		BK virus (hemorrhagic cystitis)
		Respiratory viruses

Early Post-engraftment Period (day 30 – day 100)

Cell-mediated immune suppression (acute GVHD prophylaxis and treatment)	}	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>N. meningitidis</i>
Hypogammaglobulinemia		<i>Listeria monocytogenes</i>
		<i>Nocardia</i>
		<i>Pneumocystis jirovecii</i>
		<i>Aspergillus</i> species
		Other molds
		CMV
		HHV-6
		Adenovirus
		Respiratory viruses

Chronic GVHD: prolonged risk of post-engraftment infections

FIGURE 102-1 Timing of infection after hematopoietic stem cell transplantation. CMV, Cytomegalovirus; GVHD, graft-versus-host disease; HHV, human herpesvirus; HSV, herpes simplex virus; IV, intravenous.