TABLE 169-1 RISK OF INFECTION, BY TYPE OF HEMATOPOIETIC STEM CELL TRANSPLANT

Type of Hematopoietic Stem Cell Transplant	Source of Stem Cells	Risk of Early Infection: Neutrophil Depletion	Risk of Late Infection: Impaired T and B Cell Function	Risk of Ongoing Infection: GVHD and Iatrogenic Immunosuppression	Graft vs. Tumor Effect
Autologous	Recipient (self)	High risk; neutrophil recovery sometimes prolonged	~1 year	Minimal to no risk of GVHD and late-onset severe infection	None (–)
Syngeneic (genetic twin)	Identical twin	Low risk; 1–2 weeks for neutrophil recovery	~1 year	Minimal risk of GVHD and late-onset severe infection	+/–
Allogeneic related	Sibling	Low risk; 1–2 weeks for neutrophil recovery	~1 year	Minimal to moderate risk of GVHD and late-onset severe infection	++
Allogeneic related	Child/parent (haploidentical)	Intermediate risk; 2–3 weeks for neutrophil recovery	1–2 years	Moderate risk of GVHD and late-onset severe infection	++++
Allogeneic unrelated adult	Unrelated donor	Intermediate risk; 2–3 weeks for neutrophil recovery	1–2 years	High risk of GVHD and late-onset severe infection	++++
Allogeneic unrelated cord blood	Unrelated cord-blood units (×2)	Intermediate to high risk; neutrophil recovery sometimes prolonged	Prolonged	Minimal to moderate risk of GVHD and late-onset severe infection	++++
Allogeneic mini (nonmyeloablative)	Donor (transiently coexisting with recipient cells)	Low risk; neutrophil counts close to normal	1–2+ years	Variable risk of GVHD and late-onset severe infection[a]	++++ (but develops slowly)

[a]Depending on the disparity of the match (major and minor histocompatibility antigens), GVHD may be severe or mild, the requirement for immunosuppression intense or minimal, and the risk of severe late infections coordinate with the degree of immunosuppression.

Abbreviation: GVHD, graft-versus-host disease.

Beyond the first few days of neutropenia, infections with nosocomial pathogens (e.g., vancomycin-resistant enterococci, *Stenotrophomonas maltophilia*, *Acinetobacter* species, and extended-spectrum β-lactamase–producing gram-negative bacteria) as well as with filamentous bacteria (e.g., *Nocardia* species) become more common. Vigilance is indicated, particularly for patients with a history of active or known latent tuberculosis, even when they have been appropriately pretreated. A form of bacterial colitis among cord-blood recipients has occurred 90–300 days after transplantation, responds to antimicrobial agents such as metronidazole, and—as determined by polymerase chain reaction (PCR) of biopsy specimens—may be attributed to the bacterium *Bradyrhizobium enterica* (related to *B. japonicum*). Episodes of bacteremia due to encapsulated organisms mark the late posttransplantation period (>6 months after HSC reconstitution); patients who have undergone splenectomy and those with persistent hypogammaglobulinemia are at particular risk.

FUNGAL INFECTIONS

Beyond the first week after transplantation, fungal infections become increasingly common, particularly among patients who have received broad-spectrum antibiotics. As in most granulocytopenic patients, *Candida* infections are most commonly seen in this setting. However, with increased use of prophylactic fluconazole, infections with resistant fungi—in particular, *Aspergillus* and other non-*Aspergillus* molds (*Rhizopus*, *Fusarium*, *Scedosporium*, *Penicillium*)—have become more common, prompting some centers to replace fluconazole with agents such as micafungin, voriconazole, or posaconazole. The role of antifungal prophylaxis with these different agents, in contrast to empirical treatment for suspected infection that is based on a positive β-D-glucan assay or galactomannan antigen test, remains controversial (Chap. 104). Documented infection should be aggressively treated, ideally with agents of proven activity. In patients with GVHD who require prolonged or indefinite courses of glucocorticoids and other immunosuppressive agents (e.g., cyclosporine, tacrolimus [FK 506, Prograf], mycophenolate mofetil [Cellcept], rapamycin [sirolimus, Rapamune], antithymocyte globulin, or anti-CD52 antibody [alemtuzumab, Campath—an antilymphocyte and antimonocyte monoclonal antibody]), there is a high risk of fungal infection (usually with *Candida* or *Aspergillus*) even after engraftment and resolution of neutropenia. These patients are also at high risk for reactivation of latent fungal infection (histoplasmosis, coccidioidomycosis, or blastomycosis) in areas where endemic fungi reside and after involvement

TABLE 169-2 COMMON SOURCES OF INFECTIONS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

	Period after Transplantation		
Infection Site	Early (<1 Month)	Middle (1–4 Months)	Late (>6 Months)
Disseminated	Aerobic bacteria (gram-negative, gram-positive)	*Candida, Aspergillus,* EBV	Encapsulated bacteria (*Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitidis*)
Skin and mucous membranes	HSV	HHV-6	VZV, HPV (warts)
Lungs	Aerobic bacteria (gram-negative, gram-positive), *Candida, Aspergillus,* other molds, HSV	CMV, seasonal respiratory viruses, *Pneumocystis, Toxoplasma*	*Pneumocystis, Nocardia, S. pneumoniae*
Gastrointestinal tract	*Clostridium difficile*	CMV, adenovirus, *Bradyrhizobium enterica* (cord blood cells)	EBV, CMV, *B. enterica* (cord blood cells)
Kidney		BK virus, adenovirus	
Brain		HHV-6, *Toxoplasma*	*Toxoplasma,* JC virus (rare)
Bone marrow		CMV, HHV-6	CMV, HHV-6

Abbreviations: CMV, cytomegalovirus; EBV, Epstein-Barr virus; HHV-6, human herpesvirus type 6; HPV, human papillomavirus; HSV, herpes simplex virus; VZV, varicella-zoster virus.