essential for positive early outcomes. Rarely, donor-transmitted infections can occur, including viral pathogens such as rabies virus, West Nile virus, lymphocytic choriomeningitis virus (LCMV), HIV, and hepatitis B and C viruses. Organ banks and transplantation centers continue to work to improve the sensitivity and specificity of donor testing paradigms to prevent transmission of infection.

The most common time for opportunistic infections such as CMV, *Listeria*, *Legionella*, and invasive fungal infections such as *Aspergillus* is 1 to 6 months after transplantation. Later infection may be seen in those receiving lymphocyte-depleting induction agents (e.g., thymoglobulin, alemtuzumab) to prevent acute rejection at the time of transplantation or in those with episodes of acute rejection.

Because CMV causes symptomatic infection and is associated with chronic allograft dysfunction, prophylaxis or preemptive treatment of infection with valganciclovir is used. Seronegative recipients of a CMV-seropositive organ are at highest risk for infection. Lung transplant recipients, who are at significant risk for *Aspergillus* infection in the first 6 months after transplantation, receive prophylactic voriconazole to prevent invasive fungal infection. Lung recipients are at lifelong risk for respiratory viral infections. Lung transplant recipients may also receive azithromycin to improve the prognosis for bronchiolitis obliterans syndrome, the most common manifestation of chronic allograft dysfunction.

Heart transplant recipients are at particular risk for reactivation of donor-transmitted infection with *Toxoplasma gondii*, which can cause early myocarditis or late cerebral disease. Serologic (IgG) screening of the donor and recipient, with sulfamethoxazole-trimethoprim prophylaxis used in seropositive recipients or seronegative recipients of a seropositive heart, is the standard of care in cardiac transplantation centers.

P. jirovecii can cause infection in solid organ transplant recipients, which usually occurs 6 to 12 months after transplantation. Pneumonitis similar to that seen in patients with HIV is the most common manifestation, although extrapulmonary infection (particularly in the liver and spleen) can be seen in transplant recipients. Prophylaxis with sulfamethoxazole-trimethoprim (or atovaquone in sulfa-allergic patients) is indicated for 12 months after transplantation. If high-dose corticosteroids or antilymphocyte therapy is required for treatment of acute rejection, prophylaxis should be restarted.

Almost all liver transplant recipients with underlying active hepatitis B or C have reactivation of the infection. Treatment of hepatitis B with lamivudine or other antiviral agents is often successful in suppressing infection when started at the time of transplantation. Although more difficult, post-transplantation treatment of symptomatic hepatitis C with interferon, ribavirin, and protease inhibitors may prolong hepatic function. Newer direct acting agents are being studied in the post-transplant setting.

In patients with no episodes of acute rejection, the risk of opportunistic infections often declines with time. Late infections (≥12 months after transplantation) may still occur, with varicella-zoster virus (VZV), HSV (particularly encephalitis) *Cryptococcus neoformans*, JC virus (i.e., progressive multifocal leukoencephalopathy), and community-acquired infections such as influenza and *S. pneumoniae* most commonly reported. Patients with hypogammaglobulinemia complicating long-term immunosuppressive therapy may benefit from IVIG to help prevent infections.

Although not always possible, especially with lifesaving heart, lung, or liver transplants, reduction of immunosuppression in the organ transplant recipient with invasive fungal infection, viral infection, or bacterial sepsis may assist in recovery. Reinstitution of immunosuppressive therapy may be indicated as infection resolves.

A significant challenge in treating infections in the patient with a solid organ transplant or GVHD complicating HSCT is the cytochrome P-450 metabolism of antimicrobial agents such as the azoles, macrolides, rifampin, echinocandins, nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors, and non-nucleoside reverse transcriptase inhibitors (NNRTIs). Careful monitoring of levels of calcineurin inhibitors (e.g., cyclosporine, tacrolimus) is indicated for patients on these and other agents that can induce or inhibit P-450 metabolism.

Although the immunocompromised patient may not seroconvert from vaccinations such as the annual influenza vaccine, immunization of household contacts and health care workers can prevent exposure and therefore infection of the most vulnerable hosts. Immunocompromised patients should avoid live virus vaccines (e.g., measles/mumps/rubella, varicella, yellow fever) that can be associated with disseminated infection. Specialized protocols exist for immunization of immunocompromised children.

PROGNOSIS

The prognosis of infections in immunocompromised hosts relies on accurate and rapid diagnosis and early institution of appropriate antimicrobial therapy. Use of cidal therapies (versus static agents) is recommended. Manipulation of the immune response to infection through G-CSF administration (in neutropenic patients), administration of IVIG (in hypogammaglobulinemic patients), or decreasing immunosuppressive therapy (in kidney or pancreas transplant recipients) may improve survival.

The prognosis for infections in these settings is worse for older patients, those requiring intensive care unit (ICU) admission, and those in whom rapid immune reconstitution is not possible. Tumor lysis syndrome, acute respiratory failure, and sepsis increase mortality. Patients with underlying acute leukemia and those with other comorbidities, including cardiovascular disease, renal failure, liver disease, or lung disease have a significantly worse prognosis, particularly in the setting of invasive fungal infection. The attributable mortality rate for invasive aspergillosis is 20% to 50% when patients require ICU admission (Fig. 102-3).

CONCLUSIONS

Care of the immunocompromised host with infection requires meticulous monitoring of symptoms, detection of often subtle physical findings, and an understanding of the arms of the immune system involved in a particular patient's illness. With successes in treatment of malignancies and end-organ disease, the breadth of infections causing infection in these hosts continues to widen.