prophylactic use of high doses of broad-spectrum antibiotics for the first 3–4 days after surgery may decrease the incidence of pneumonia. Gram-negative pathogens (Enterobacteriaceae and *Pseudomonas* species) are troublesome in the first 2 weeks after surgery (the period of maximal vulnerability). Pneumonia can also be caused by *Candida* (possibly as a result of colonization of the donor lung), *Aspergillus*, and *Cryptococcus.* Many centers use antifungal prophylaxis (typically fluconazole or liposomal amphotericin B) for the first 1–2 weeks.

Mediastinitis may occur at an even higher rate among lung transplant recipients than among heart transplant recipients and most commonly develops within 2 weeks of surgery. In the absence of prophylaxis, pneumonitis due to CMV (which may be transmitted as a consequence of transplantation) usually presents between 2 weeks and 3 months after surgery, with primary disease occurring later than reactivation disease.

Middle-Period Infections The incidence of CMV infection, either reactivated or primary, is 75–100% if either the donor or the recipient is seropositive for CMV. CMV-induced disease after solid organ transplantation appears to be most severe in recipients of lung and heart-lung transplants. Whether this severity relates to the mismatch in lung antigen presentation and host immune cells or is attributable to nonimmunologic factors is not known. More than half of lung transplant recipients with symptomatic CMV disease have pneumonia. Difficulty in distinguishing the radiographic picture of CMV infection from that of other infections or from organ rejection further complicates therapy. CMV can also cause bronchiolitis obliterans in lung transplants. The development of pneumonitis related to HSV has led to the prophylactic use of acyclovir. Such prophylaxis may also decrease rates of CMV disease, but ganciclovir is more active against CMV and is also active against HSV. The prophylaxis of CMV infection with IV ganciclovir—or increasingly with valganciclovir, the oral alternative—is recommended for lung transplant recipients. Antiviral alternatives are discussed in the earlier section on HSC transplantation. Although the overall incidence of serious disease is decreased during prophylaxis, late disease may occur when prophylaxis is stopped—a pattern observed increasingly in recent years. With recovery from peritransplantation complications and, in many cases, a decrease in immunosuppression, the recipient is often better equipped to combat late infection.

Late Infections The incidence of *Pneumocystis* infection (which may present with a paucity of findings) is high among lung and heart-lung transplant recipients. Some form of prophylaxis for *Pneumocystis* pneumonia is indicated in all organ transplant situations (Table 169-5). Prophylaxis with TMP-SMX for 12 months after transplantation may be sufficient to prevent *Pneumocystis* disease in patients whose immunosuppression is not increased.

As in other transplant recipients, EBV infection in lung and heart-lung recipients may cause either a mononucleosis-like syndrome or EBV-LPD. The tendency of the B cell blasts to present in the lung appears to be greater after lung transplantation than after the transplantation of other organs, possibly because of a rich source of B cells in bronchus-associated lymphoid tissue. Reduction of immunosuppression and switching of regimens, as discussed in earlier sections, cause remission in some cases, but mTor inhibitors such as rapamycin may contribute to lung toxicity. Airway compression can be fatal, and rapid intervention may therefore become necessary. The approach to EBV-LPD is similar to that described in other sections.

LIVER TRANSPLANTATION

Early Infections As in other transplantation settings, early bacterial infections are a major problem after liver transplantation. Many centers administer systemic broad-spectrum antibiotics for the first 24 h or sometimes longer after surgery, even in the absence of documented infection. However, despite prophylaxis, infectious complications are common and correlate with the duration of the surgical procedure and the type of biliary drainage. An operation lasting >12 h is associated with an increased likelihood of infection. Patients who have a choledochojejunostomy with drainage of the biliary duct to a Roux-en-Y jejunal bowel loop have more fungal infections than those whose bile is drained via anastomosis of the donor common bile duct to the recipient common bile duct. Overall, liver transplant patients have a high incidence of fungal infections, and the occurrence of fungal (often candidal) infection in the setting of choledochojejunostomy correlates with retransplantation, elevated creatinine levels, long procedures, transfusion of >40 units of blood, reoperation, preoperative use of glucocorticoids, prolonged treatment with antibacterial agents, and fungal colonization 2 days before and 3 days after surgery. Many centers give antifungal agents prophylactically in this setting.

Peritonitis and intraabdominal abscesses are common complications of liver transplantation. Bacterial peritonitis or localized abscesses may result from biliary leaks. Early leaks are especially common with live-donor liver transplants. Peritonitis in liver transplant recipients is often polymicrobial, frequently involving enterococci, aerobic gram-negative bacteria, staphylococci, anaerobes, or *Candida* and sometimes involving other invasive fungi. Only one-third of patients with intraabdominal abscesses have bacteremia. Abscesses within the first month after surgery may occur not only in and around the liver but also in the spleen, pericolic area, and pelvis. Treatment includes antibiotic administration and drainage as necessary.

Middle-Period Infections The development of postsurgical biliary stricture predisposes patients to cholangitis. The incidence of strictures is increased in live-donor liver transplantation. Transplant recipients who develop cholangitis may have high spiking fevers and rigors but often lack the characteristic signs and symptoms of classic cholangitis, including abdominal pain and jaundice. Although these findings may suggest graft rejection, rejection is typically accompanied by marked elevation of liver function enzymes. In contrast, in cholangitis in transplant recipients, results of liver function tests (with the possible exception of alkaline phosphatase levels) are often within the normal range. Definitive diagnosis of cholangitis in liver transplant recipients requires demonstration of aggregated neutrophils in bile duct biopsy specimens. Unfortunately, invasive studies of the biliary tract (either T-tube cholangiography or endoscopic retrograde cholangiopancreatography) may themselves lead to cholangitis. For this reason, many clinicians recommend an empirical trial of therapy with antibiotics covering gram-negative organisms and anaerobes before these procedures are undertaken as well as antibiotic coverage if procedures are eventually performed.

Reactivation of viral hepatitis is a common complication of liver transplantation (Chap. 360). Recurrent hepatitis B and C infections, for which transplantation may be performed, are problematic. To prevent hepatitis B virus reinfection, prophylaxis with an optimal antiviral agent or combination of agents (lamivudine, adefovir, entecavir) and hepatitis B immune globulin is currently recommended, although the optimal dose, route, and duration of therapy remain controversial. Success in preventing reinfection with hepatitis B virus has increased in recent years. Complications related to hepatitis C infection are the most common reason for liver transplantation in the United States. Reinfection of the graft with hepatitis C virus occurs in all patients, with a variable time frame. Studies of aggressive pretransplantation treatment of selected recipients with antiviral agents and prophylactic/preemptive regimens are ongoing. However, early posttransplantation initiation of treatment for histologically documented disease with the classic combination of ribavirin and pegylated interferon has produced sustained responses at rates in the range of 25–40%. Several protease and polymerase inhibitors that block production of hepatitis C virus as well as regimens that spare interferon and a monoclonal antibody to the virus are undergoing preclinical and clinical trials for prevention and or control of infection after transplantation (Chap. 360).

As in other transplantation settings, reactivation disease with herpesviruses is common (Table 169-3). Herpesviruses can be transmitted in donor organs. Although CMV hepatitis occurs in ~4% of liver transplant recipients, it is usually not so severe as to require retransplantation. Without prophylaxis, CMV disease develops in the majority of seronegative recipients of organs from CMV-positive donors, but fatality rates are lower among liver transplant recipients than among lung or heart-lung transplant recipients. Disease due to CMV can also