

both lungs of the recipient must be replaced to remove the reservoir of infection.

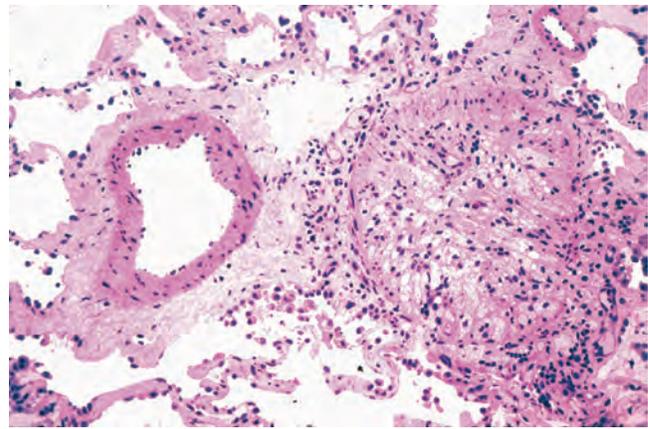
With improving surgical and organ preservation techniques, postoperative complications (e.g., anastomotic dehiscence, vascular thrombosis, primary graft dysfunction) are fortunately becoming rare. The transplanted lung is subject to two major complications: infection and rejection.

- **Pulmonary infections** in lung transplant patients are essentially those of any immunocompromised host, discussed earlier. In the early posttransplant period (the first few weeks), bacterial infections are most common. With ganciclovir prophylaxis and matching of donor-recipient CMV status, CMV pneumonia occurs less frequently and is less severe, although some resistant strains are emerging. Most infections occur in the third to twelfth month after transplantation. *Pneumocystis jiroveci* pneumonia is rare, since almost all patients receive adequate prophylaxis, usually with Bactrim (trimethoprim-sulfamethoxazole). Fungal infections are mostly due to *Aspergillus* and *Candida* species, and they involve the bronchial anastomotic site and/or the lung.
- **Acute rejection** of the lung occurs to some degree in all patients despite routine immunosuppression. It most often appears several weeks to months after surgery but also may present years later or whenever immunosuppression is decreased. Patients present with fever, dyspnea, cough, and radiologic infiltrates. Since these are similar to the picture of infections, diagnosis often relies on transbronchial biopsy.
- **Chronic rejection** is a significant problem in at least half of all patients by 3 to 5 years posttransplant. It is manifested by cough, dyspnea, and an irreversible decrease in lung function tests due to pulmonary fibrosis.

## MORPHOLOGY

The morphologic features of acute rejection are primarily those of inflammatory infiltrates (lymphocytes, plasma cells, and few neutrophils and eosinophils), either around small vessels, in the submucosa of airways, or both. The major morphologic correlate of chronic rejection is **bronchiolitis obliterans**, the partial or complete occlusion of small airways by fibrosis, with or without active inflammation (Fig. 15-40). Bronchiolitis obliterans is patchy and therefore difficult to diagnose via transbronchial biopsy. Bronchiectasis and pulmonary fibrosis may develop in long-standing cases.

Acute cellular airway rejection (the presumed forerunner of later, fibrous obliteration of these airways) is generally responsive to therapy, but the treatment of established bronchiolitis obliterans has been disappointing. Its progress may be slowed or even halted for some time, but it cannot be reversed. Infrequent complications of lung transplantation include accelerated pulmonary arteriosclerosis in the graft and EBV-associated B cell lymphoma. With continuing improvement in surgical, immunosuppressive, and antimicrobial therapies, the short-term outcome of lung transplantation has improved considerably, although it is still not as good as that for renal or cardiac



**Figure 15-40** Chronic rejection of lung allograft associated with bronchiolitis obliterans. An adjacent pulmonary artery is normal. (Courtesy of Dr. Thomas Krausz, Department of Pathology, The University of Chicago, Pritzker School of Medicine, Chicago, IL.)

transplantation. One-, five-, and ten-year survival rates are 79%, 53%, and 30%, respectively.

## Tumors

A variety of benign and malignant tumors may arise in the lung, but 90% to 95% are carcinomas, about 5% are bronchial carcinoids, and 2% to 5% are mesenchymal and other miscellaneous neoplasms.

## Carcinomas

**Lung cancer is currently the most frequently diagnosed major cancer in the world** (estimated 1.6 million new cases in 2008) and **the most common cause of cancer mortality worldwide** (1,380,000 deaths in 2008). This is largely due to the carcinogenic effects of cigarette smoke. Over the coming decades, changes in smoking habits will greatly influence lung cancer incidence and mortality as well as the prevalence of various histologic types of lung cancer.

The number of new cases of lung cancer occurring in 2012 in the United States was estimated to be 226,160 (note that in 1950 it was 18,000), accounting for about 14% of cancer diagnoses and 160,340 deaths, roughly 28% of all cancer-related deaths. As can be gathered from the sobering fact that the yearly mortality almost matches the yearly incidence, the overall outlook for affected patients remains bleak. Since the early 1990s, lung cancer incidence and mortality rates have been decreasing in men, due to the decreased smoking rates over the past 35 years. However, decreases in smoking patterns among women lag behind those of men. Since 1987 more women have died each year of lung cancer than of breast cancer, which for more than 40 years had been the major cause of cancer death in women. Cancer of the lung occurs most often between ages 40 and 70 years, with a peak incidence in the 50s or 60s. Only 2% of all cases appear before the age of 40.

**Etiology and Pathogenesis.** Most (but not all) lung cancers are associated with a well-known carcinogen—cigarette smoke. In addition there are other genetic and environmental factors which we will discuss after the role of