lobe disease who have a low exercise tolerance despite rehabilitation and are without other major comorbidities. This subgroup may have reduced mortality after LVRS (level 2 evidence). In general, a high surgical mortality risk exists in patients referred for LVRS who have an FEV_1 or DLCO of less than 20% predicted and in those who have more homogeneous distribution of emphysema. Endoscopic therapies to deflate regions of lung with emphysema are currently under investigation.

Single or bilateral lung transplantation is an option for patients with end-stage airflow obstruction. The average survival after lung transplantation is 4 to 5 years. Rejection, viral infections, transplant-associated lymphoproliferative disease, and late occurrence of bronchiolitis obliterans remain significant problems, but the procedure can improve the quality of life in properly selected patients.

Palliative Care

Although the disease course can be unpredictable, discussion of end-of-life issues with the patient is an important component of longitudinal care as COPD progresses to an advanced stage. Preparation of advance directives regarding use of intensive care measures at the end of life may be desirable. Opioid narcotics can be highly effective for relieving dyspnea in patients with terminal complications of COPD (level 1 evidence).

Prognosis

COPD is a chronic and progressive disease with a variable and typically prolonged clinical course. As discussed previously, measurement of lung function (FEV_1 % predicted) has prognostic significance, and use of the multifactorial BODE index can improve prognostication compared with use of FEV_1 alone. Patients who have frequent exacerbations of COPD appear to have more rapid loss of lung function than those without exacerbations, suggesting that frequent exacerbations result in a worse clinical course.

At present, aside from smoking cessation and the addition of long-term oxygen therapy for patients with hypoxemia, interventions to improve survival in COPD are limited. No pharmacologic therapy for COPD has been definitively demonstrated to improve survival. In mild COPD, mortality is frequently related to comorbidities such as ischemic heart disease and lung cancer; in more advanced stages, a greater proportion of patients die from respiratory causes.

BRONCHIOLAR DISORDERS

Definition and Epidemiology

The bronchioles are defined as the small noncartilaginous airways (<2 mm in diameter). The bronchiolar disorders, or bronchiolitides, encompass a spectrum of diseases of widely varying causes primarily affecting these small airways. Although small airways disease contributes significantly to the syndrome of COPD, and respiratory bronchiolitis may be found incidentally in smokers, bronchiolar disorders with different etiologies than cigarette smoking also exist. These disorders are associated with patchy inflammation and epithelial injury, fibrosis, mucoid impaction, or obliteration of the bronchioles (E-Fig. 16-8). These changes result in airflow limitation due to increased airway resistance.

Acute bronchiolitis related to respiratory syncytial virus infection is epidemic among infants and young children, but primary bronchiolar disorders, including infectious or postinfectious bronchiolitis, are rare in the adult general population and tend to affect certain specific patient populations.

Pathology

The pathology of the bronchiolar disorders is complex. A variety of terms are used to describe or classify the various histopathologic patterns of small airways disease, including *cellular bronchiolitis* (inflammatory cell infiltration of the small airway wall resulting in small airway narrowing), *follicular bronchiolitis* (formation of abundant lymphoid follicles in close apposition to the small airways, resulting in airway compression), *obliterative* or *constrictive bronchiolitis* (fibrosis surrounding the small airways resulting in narrowing of the affected airways), and *bronchiolitis obliterans* (formation of endoluminal fibrous lesions, sometimes called *Masson bodies*, obstructing the small airway lumen). The histopathologic pattern of small airways disease may suggest a likely underlying etiology; for example, follicular bronchiolitis is often, although not exclusively, seen in the context of Sjögren's syndrome.

Clinical Presentation

In general, the bronchiolar disorders manifest nonspecifically with dyspnea, which may be severe or progressive, in some cases accompanied by cough or sputum production. The physical examination may reveal inspiratory squeaks or wheezes but may be surprisingly normal. The possibility of a bronchiolar disorder should be considered in particular settings. For example, bronchiolitis may complicate the course of rheumatoid arthritis, Sjögren's syndrome, or inflammatory bowel disease.

Diffuse panbronchiolitis is a rare idiopathic disorder, most common in Japan, that is characterized by cough with purulent sputum, sinusitis, and dyspnea. Recurrent respiratory infections with bacterial organisms such as *Pseudomonas aeruginosa* complicate the course of diffuse panbronchiolitis. Bronchiolitis obliterans (in this context a clinical, not a histopathologic, term) is seen with the bronchiolitis obliterans syndrome of chronic allograft rejection after lung transplantation, in graft-versus-host disease after allogeneic hematopoietic stem cell transplantation, and after occupational toxin exposures. For example, occupational clusters of bronchiolitis obliterans have been described after exposure to diacetyl, a flavoring chemical used in the manufacture of microwave popcorn.

Diagnosis and Differential Diagnosis

In general, the bronchiolar disorders cause an obstructive pattern of expiratory airflow limitation on pulmonary function testing without evidence of reversibility. The bronchiolitis obliterans syndrome is diagnosed clinically by a decline in FEV_1 of 20% from a stable baseline value on serial testing after lung transplantation. HRCT is valuable in the diagnosis and assessment of the bronchiolar disorders. Characteristic findings on HRCT include centrilobular nodules or tree-in-bud opacities, reflecting impacted inflammatory exudates or sloughed epithelial cells in the bronchioles. A "mosaic attenuation" pattern, with decreased attenuation in geographic regions of lung reflecting areas of air trapping