to oxygen therapy due to ventilation perfusion mismatching (described below), and respiratory acidosis can develop. Early in the course, the lungs become stiff due to loss of functional surfactant.

The functional abnormalities in ALI are not evenly distributed throughout the lungs. The lungs have areas that are infiltrated, consolidated, or collapsed (and thus poorly aerated and poorly compliant) and regions that have nearly normal levels of compliance and ventilation. Poorly aerated regions continue to be perfused, producing *ventilation-perfusion mismatch* and hypoxemia.

There are no proven specific treatments; however, due to improvements in therapy for sepsis, mechanical ventilation, and supportive care, the mortality rate among the 200,000 ALI/ARDS cases seen yearly in the United States has decreased from 60% to about 40%, with the majority of deaths attributable to sepsis or multiorgan failure and, in some cases, direct lung injury. Most survivors recover pulmonary function but many have persistent impairment in physical and cognitive functions. In a minority of patients, the exudate and diffuse tissue destruction result in scarring, interstitial fibrosis, and chronic pulmonary disease.

KEY CONCEPTS

Acute Respiratory Distress Syndrome

- ARDS is a clinical syndrome of progressive respiratory insufficiency caused by diffuse alveolar damage in the setting of sepsis, severe trauma, or diffuse pulmonary infection.
- Damage to endothelial and alveolar epithelial cells, with inflammation, are the key initiating events and the basis of lung damage.
- The characteristic histologic picture is that of hyaline membranes lining alveolar walls. Edema, scattered neutrophils and macrophages, and epithelial necrosis are also present.

Acute Interstitial Pneumonia

Acute interstitial pneumonia is a term that is used to describe widespread ALI of unknown etiology associated with a rapidly progressive clinical course. It is sometimes referred to as idiopathic ALI-DAD. It is an uncommon disorder that occurs at a mean age of 59 years and has no sex predilection. Patients present with acute respiratory failure often following an illness of less than 3 weeks' duration that resembles an upper respiratory tract infection. The radiographic and pathologic features are identical to those of the organizing stage of ALI. The mortality rate varies from 33% to 74%, with most deaths occurring within 1 to 2 months. Recurrences and chronic interstitial disease may occur in the survivors.

Obstructive and Restrictive Lung Diseases

Obstructive lung diseases (or airway diseases) are characterized by an increase in resistance to airflow due to partial or complete obstruction at any level from the trachea and larger bronchi to the terminal and respiratory bronchioles. These are contrasted with restrictive diseases, which are characterized by reduced expansion of lung parenchyma and decreased total lung capacity. The distinction between these chronic noninfectious diffuse pulmonary diseases is based primarily on pulmonary function tests. In individuals with diffuse obstructive disorders, pulmonary function tests show decreased maximal airflow rates during forced expiration, usually expressed as the forced expiratory volume at 1 second (FEV_1) over the forced ventilatory capacity (FVC). An FEV_1/FVC ratio of less than 0.7 generally indicates airway obstruction. Expiratory airflow obstruction may be caused by a variety of conditions (Table 15-3) that are ideally distinguished by distinct pathologic changes and different mechanisms of airflow obstruction. As discussed later, however, such neat distinctions are not always possible. In contrast, restrictive diseases are associated with proportionate decreases in both total lung capacity and FEV_1, leading to normal FEV_1/FVC ratio. Restrictive defects occur in two broad kinds of conditions: (1) *chest wall disorders* (e.g., severe obesity, pleural diseases, kyphoscoliosis, and neuromuscular diseases such as poliomyelitis) and (2) *chronic interstitial and infiltrative diseases*, such as pneumoconioses and interstitial fibrosis.

Obstructive Lung Diseases

Common obstructive lung diseases include emphysema, chronic bronchitis, asthma, and bronchiectasis, each of which has distinct pathologic features and clinical characteristics (Table 15-3). Emphysema and chronic bronchitis are often clinically grouped together and referred to as *chronic obstructive pulmonary disease* (COPD), since the majority of patients have features of both, almost certainly because they share a major trigger—cigarette

Table 15-3 Disorders Associated with Airflow Obstruction: The Spectrum of Chronic Obstructive Pulmonary Disease

Clinical Term	Anatomic Site	Major Pathologic Changes	Etiology	Signs/Symptoms
Chronic bronchitis	Bronchus	Mucous gland hyperplasia, hypersecretion	Tobacco smoke, air pollutants	Cough, sputum production
Bronchiectasis	Bronchus	Airway dilation and scarring	Persistent or severe infections	Cough, purulent sputum, fever
Asthma	Bronchus	Smooth muscle hyperplasia, excess mucus, inflammation	Immunologic or undefined causes	Episodic wheezing, cough, dyspnea
Emphysema	Acinus	Airspace enlargement; wall destruction	Tobacco smoke	Dyspnea
Small-airway disease, bronchiolitis*	Bronchiole	Inflammatory scarring/obliteration	Tobacco smoke, air pollutants, miscellaneous	Cough, dyspnea

*Can be seen with any form of obstructive lung disease or as an isolated finding.