ACUTE LUNG INJURY

Acute lung injury in its most severe form is called *acute respiratory distress syndrome* (ARDS). It typically manifests with dyspnea, cyanosis, tachypnea, tachycardia, diaphoresis, and diffuse crackles detected on examination. ARDS is characterized by increased permeability of the alveolar-capillary membrane, leading to flooding of the alveolar spaces with proteinaceous edema fluid. It is defined by clinical measures of the severity of lung dysfunction (e.g., PaO_2/FIO_2 ratio).

Based on the 2012 revised Berlin definition of ARDS, the severity can be separated into mild, moderate, and severe forms. Mild ARDS requires the Pao_2/FIO_2 ratio to be between 200 and 300 mm Hg on ventilator settings (PEEP or CPAP ≥5 cm H_2O). Moderate or severe ARDS occurs when the PaO_2/FIO_2 ratio is between 100 and 200 mm Hg or 100 mm Hg or less on ventilator settings (PEEP or CPAP ≥5 cm H_2O). Respiratory failure must not be caused by cardiac failure or fluid overload; bilateral opacities representing pulmonary edema on the chest radiograph or CT must be evident; and respiratory symptoms must be of sudden onset due to a known clinical insult (<1 week). Additional criteria include exclusion of cardiogenic pulmonary edema and other causes of acute hypoxemic respiratory failure such as idiopathic pulmonary fibrosis, chronic interstitial lung disease, and diffuse alveolar hemorrhage.

ARDS is triggered by direct injury to the lung, as observed in aspiration pneumonia, smoke inhalation, and near-drowning, or by systemic injury, such as trauma, surgery, sepsis, burns, long bone fractures, pancreatitis, uremia, transfusion therapy, shock, drug intoxication, and cardiopulmonary bypass. About 150,000 cases of ARDS are reported each year in the United States, and aspiration pneumonia and sepsis are the most common associated conditions. The morbidity rate associated with ARDS is high, and 30% to 50% of patients die.

ARDS is the pulmonary manifestation of a systemic disorder that triggers a dysregulated inflammatory response. Uncontrolled inflammation injures the pulmonary vascular endothelium, resulting in increased permeability and allowing extravasation of proteinaceous edema fluid from the intravascular space and its accumulation in the lung interstitium and alveolar spaces (E-Fig. 22-1). Injury to the lung epithelium decreases absorption of water from the alveolar space and causes secretion of abnormal or inadequate quantities of surfactant.

ARDS is often referred to as noncardiogenic or increased permeability pulmonary edema. In the lung, these processes cause right-to-left intrapulmonary shunting of blood that results in refractory hypoxemia and decreased lung compliance that increases the work of breathing. The chest radiograph reveals diffuse bilateral alveolar infiltrates (E-Fig. 22-2). Failure of other organs occurs frequently, and multiorgan failure is common, especially in the setting of sepsis.

Histologically, ARDS is characterized by diffuse alveolar damage with hyaline membranes (E-Fig. 22-3). The damage is further exaggerated by reductions in the quantity and quality of the synthesized surfactant, leading to atelectasis. After a few days, the tissue shows hyperplasia of type II pneumocytes (E-Fig. 22-4) and deposition of connective tissue resulting in fibrosis. These events can be worsened by mechanical ventilation through high tidal volumes, hyperdistention, and hyperoxia.

The diagnosis of ARDS should be considered in patients with a predisposing condition (e.g., sepsis), bilateral pulmonary infiltrates on the chest radiograph, and refractory hypoxemia (i.e., usually a Pao_2/Fio_2 ratio of 200 mm Hg or less) in the absence of significant cardiac dysfunction. Treatment of ARDS relies on supportive measures directed at eradicating the triggering event, sustaining the cardiovascular system, providing nutrition, and avoiding fluid overload. The Fluid and Catheter Treatment Trial (FACTT) conducted by the National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network showed that conservative fluid strategy resulted in more ventilator-free (2.5 days) and ICU-free days (2.2 days) than a more liberal fluid management approach (level I evidence). A ventilatory management strategy delivering low tidal volumes (about 6 mL/kg of body weight) increased survival (level I).

Advances in extracorporeal membrane oxygenation (ECMO) and pumpless extracorporeal lung assist (PECLA) have been reported, questioning the previous failures of these devices in patients with acute lung injury. The CESAR trial, which compared conventional ventilatory support with ECMO for severe respiratory failure, showed a significant improvement in survival with decreased disability at 6 months for the patients receiving ECMO (level I evidence). ECMO improved mortality for younger patients with H1N1-induced ARDS (level II-2). Several observational and uncontrolled clinical trials have shown similar improvements in survival rates. However, hemolysis and anticoagulation complications have restricted the use of ECMO.

High-frequency oscillatory ventilation (HFOV) has also been tried in patients with moderate to severe ARDS, but the mortality rate was not reduced, and there were worse outcomes than with conventional positive-pressure ventilation. Corticosteroids, surfactant replacement, and extracorporeal oxygenation have not proved beneficial and are not recommended. Oxygenation can be improved by PEEP and prone ventilation, but these interventions do not improve mortality rates. There was no difference in the 60-day mortality rate or improvement in ventilator-free days between initial trophic and full enteral feeding (EDEN trial, level I evidence). Early and late enteral feeding also showed no difference in mortality rates. Antioxidants, omega-3 fatty acids, and γ-linolenic acid did not improve clinical outcomes in patients with acute lung injury. Because there is no available therapy that lessens acute lung injury or hastens repair, the key to care of patients with ARDS is meticulous supportive care and avoidance of complications such as ventilator-associated pneumonia or catheter-related sepsis.

The lung injury prediction score (LIPS) encompasses various predisposing conditions and risk modifiers that have been found useful as a screening tool (negative predictive value −0.97) in clinical trials (level A evidence). As a result, such prognostic measures in identifying patients at risk of acute lung injury or ARDS on admission may lead to interventions that prevent disease progression or allow for close monitoring of patients for disease progression.

Most patients who survive ARDS do not have significant pulmonary function abnormalities in 12 months. The most common