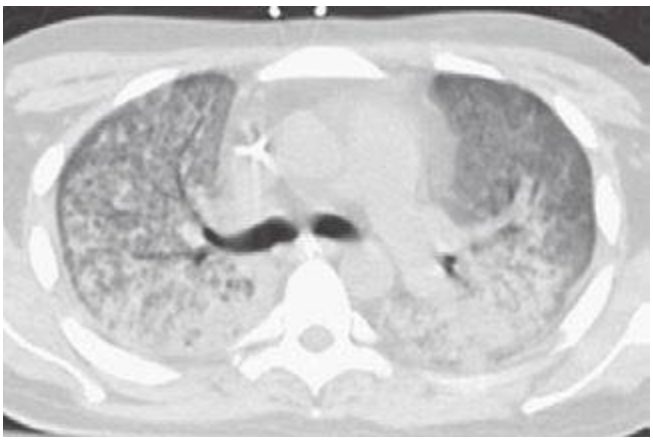

FIGURE 322-4 A representative CT scan of the chest during the exudative phase of ARDS, in which *dependent* alveolar edema and atelectasis predominate.

ventilation during this phase. Despite this improvement, many patients still experience dyspnea, tachypnea, and hypoxemia. Some patients develop progressive lung injury and early changes of pulmonary fibrosis during the proliferative phase. Histologically, the first signs of resolution are often evident in this phase, with the initiation of lung repair, the organization of alveolar exudates, and a shift from a neutrophil- to a lymphocyte-predominant pulmonary infiltrate. As part of the reparative process, type II pneumocytes proliferate along alveolar basement membranes. These specialized epithelial cells synthesize new pulmonary surfactant and differentiate into type I pneumocytes.

Fibrotic Phase While many patients with ARDS recover lung function 3–4 weeks after the initial pulmonary injury, some enter a fibrotic phase that may require long-term support on mechanical ventilators and/or supplemental oxygen. Histologically, the alveolar edema and inflammatory exudates of earlier phases are now converted to extensive alveolar-duct and interstitial fibrosis. Marked disruption of acinar architecture leads to emphysema-like changes, with large bullae. Intimal fibroproliferation in the pulmonary microcirculation causes progressive vascular occlusion and pulmonary hypertension. The physiologic consequences include an increased risk of pneumothorax, reductions in lung compliance, and increased pulmonary dead space. Patients in this late phase experience a substantial burden of excess morbidity. Lung biopsy evidence for pulmonary fibrosis in any phase of ARDS is associated with increased mortality risk.

TREATMENT ACUTE RESPIRATORY DISTRESS SYNDROME

GENERAL PRINCIPLES

Recent reductions in ARDS mortality rates are largely the result of general advances in the care of critically ill patients **(Chap. 321)**. Thus, caring for these patients requires close attention to (1) the recognition and treatment of underlying medical and surgical disorders (e.g., sepsis, aspiration, trauma); (2) the minimization of procedures and their complications; (3) prophylaxis against venous thromboembolism, gastrointestinal bleeding, aspiration, excessive sedation, and central venous catheter infections; (4) prompt recognition of nosocomial infections; and (5) provision of adequate nutrition.

MANAGEMENT OF MECHANICAL VENTILATION

(See also Chap. 323) Patients meeting clinical criteria for ARDS frequently become fatigued from increased work of breathing and progressive hypoxemia, requiring mechanical ventilation for support.

Ventilator-Induced Lung Injury Despite its life-saving potential, mechanical ventilation can aggravate lung injury. Experimental models have demonstrated that ventilator-induced lung injury appears to require two processes: repeated alveolar overdistention and recurrent alveolar collapse. As is clearly evident from chest CT (Fig. 322-4), ARDS is a heterogeneous disorder, principally involving dependent portions of the lung with relative sparing of other regions. Because compliance differs in affected versus more "normal" areas of the lung, attempts to fully inflate the consolidated lung may lead to overdistention of and injury to the more normal areas. Ventilator-induced injury can be demonstrated in experimental models of acute lung injury, with high-tidal-volume (V_T) ventilation resulting in additional, synergistic alveolar damage.

A large-scale, randomized controlled trial sponsored by the National Institutes of Health and conducted by the ARDS Network compared low V_T ventilation (6 mL/kg of predicted body weight) to conventional V_T ventilation (12 mL/kg predicted body weight). The mortality rate was significantly lower in the low V_T patients (31%) than in the conventional V_T patients (40%). This improvement in survival represents the most substantial ARDS-mortality benefit that has been demonstrated for *any* therapeutic intervention to date.

Prevention of Alveolar Collapse In ARDS, the presence of alveolar and interstitial fluid and the loss of surfactant can lead to a marked reduction of lung compliance. Without an increase in end-expiratory pressure, significant alveolar collapse can occur at end-expiration, with consequent impairment of oxygenation. In most clinical settings, positive end-expiratory pressure (PEEP) is empirically set to minimize F_{IO_2} (inspired O_2 percentage) and maximize Pa_{O_2} (arterial partial pressure of O_2). On most modern mechanical ventilators, it is possible to construct a static pressure–volume curve for the respiratory system. The lower inflection point on the curve represents alveolar opening (or "recruitment"). The pressure at this point, usually 12–15 mmHg in ARDS, is a theoretical "optimal PEEP" for alveolar recruitment. Titration of the PEEP to the lower inflection point on the static pressure–volume curve has been hypothesized to keep the lung open, improving oxygenation and protecting against lung injury. Three large randomized trials have investigated the utility of PEEP-based strategies to keep the lung open. In all three trials, improvement in lung function was evident but overall mortality rates were not altered significantly. Until more data become available on the clinical utility of high PEEP, it is advisable to set PEEP to minimize F_{IO_2} and optimize Pa_{O_2} **(Chap. 323)**. Measurement of esophageal pressures to estimate transpulmonary pressure may help identify an optimal PEEP in some cases.

Oxygenation can also be improved by increasing mean airway pressure with *inverse-ratio ventilation*. In this technique, the inspiratory time (*I*) is lengthened so that it is longer than the expiratory time (*E*)— that is, *I:E* > 1:1. With diminished time to exhale, dynamic hyperinflation leads to increased end-expiratory pressure, similar to ventilator-prescribed PEEP. This mode of ventilation has the advantage of improving oxygenation with lower peak pressures than are required for conventional ventilation. Although inverse-ratio ventilation can improve oxygenation and can help reduce F_{IO_2} to ≤0.60, thus avoiding possible oxygen toxicity, no benefit in ARDS mortality risk has been demonstrated. Recruitment maneuvers that transiently increase PEEP to "recruit" atelectatic lung can also increase oxygenation, but a mortality benefit has not been established.

In several randomized trials, mechanical ventilation in the prone position improved arterial oxygenation, but its effect on survival and other important clinical outcomes remains uncertain. Moreover, unless the critical-care team is experienced in "proning," repositioning critically ill patients can be hazardous, leading to accidental endotracheal extubation, loss of central venous catheters, and orthopedic injury.

OTHER STRATEGIES IN MECHANICAL VENTILATION

Several additional mechanical-ventilation strategies that use specialized equipment have been tested in ARDS patients; most of these approaches have had mixed or disappointing results in adults. *High-frequency ventilation* (HFV) entails ventilating at extremely high respiratory rates (5–20 cycles per second) and low V_Ts (1–2 mL/kg). Use of *partial liquid ventilation* (PLV) with perfluorocarbon—an inert, high-density liquid that easily solubilizes oxygen and carbon