Acute respiratory distress syndrome (ARDS) is a common and devastating condition that affects 150,000 Americans each year. ARDS sometimes strikes patients who already are seriously ill with other medical conditions, but also can overwhelm previously healthy adults. A wide variety of precipitating causes, which range from infection to trauma to aspiration of gastric acid, cripple the lungs in a remarkably stereotyped manner. The alveoli flood with protein-rich edema fluid, which impairs the mechanical properties of the lung (causing severe dyspnea), blocks gas exchange (leading to profound hypoxemia), and produces diffuse infiltrates apparent on the chest radiograph (Figure 1).

The mortality rate for patients with acute respiratory distress syndrome is roughly 40 percent.

Treatment of ARDS
No specific treatments to repair the lung are yet available, despite many attempts to identify useful drugs; as a result, therapy centers on supportive care. These strategies include mechanical ventilation with PEEP and oxygen, fluid management, and measures to prevent complications. Until recently, standard ventilator settings included tidal volumes of 10 to 15 mL/kg of body weight to maintain a normal arterial partial pressure of carbon dioxide and sufficient PEEP to maintain an acceptable arterial oxygen saturation. Fluid therapy typically is guided by a pulmonary artery catheter since cardiovascular instability, the effects of PEEP, and concomitant renal failure often combine to cloud the assessment of intravascular volume.
CONTROVERSIES IN TREATMENT

Although the above supportive measures have been the standard in managing ARDS, they have not been clearly established as safe or effective, and much controversy has attended their use. For example, PEEP is potentially harmful in that it can depress cardiac output; as a result, intensive care physicians generally have attempted to use as little PEEP as possible. On the other hand, PEEP potentially is beneficial because it can prevent repeating cycles of recruitment and derecruitment of alveoli (which has been shown to amplify lung injury in animal models\(^2\)). Similar harm-and-benefit trade-offs and therefore, controversies, attend the use of fluid therapy, the goals of ventilator therapy, and the utility of the pulmonary artery catheter. For example, some have advocated liberal fluid therapy to maximize cardiac output and oxygen delivery to the tissues. Others counter that such fluid loading may further flood the lungs, and suggest that fluids should be given only sparingly. The impact of these treatments in patients can only be guessed at based on studies in the laboratory; ultimately, large human trials are needed.

THE ARDS NETWORK

To assess the impact of these controversial therapies, a large number of leading institutions in North America have joined together to form the Acute Respiratory Distress Syndrome Network (ARDSNet). Funded by the National Institutes of Health, these institutions and their investigators have sought to settle some of these fundamental controversies. The most important of the trials to be completed and published, studied the role of tidal volume.\(^3\) Until recently, mechanical ventilation of ARDS patients had been targeted to achieve relatively normal arterial blood gas values, usually relying on tidal volumes of 10 to 15 mL/kg of body weight. Since atelectasis and edema reduce aerated lung volumes in patients with ARDS, this approach typically caused high ventilator airway pressures. Several basic science and clinical studies in the last decade, however, have shown that these high pressures reflect excessive distention of alveoli. If this were true in patients, such high tidal volumes might contribute to further damage of an already crippled lung. Paradoxically, standard supportive therapy might be causing harm and even unnecessary deaths.

The ARDSNet investigators sought to compare patients who were ventilated conventionally (perhaps involving high airway pressures) with those ventilated with low tidal volumes (even if this failed to achieve the usual target of adequate gas exchange). Over a 3-year period,
861 patients with ARDS were randomized to either an initial tidal volume of 12 mL/kg of body weight, adjusted downward to yield a plateau airway pressure (measured after a 0.5 s pause at end-inspiration) less than 50 cm H₂O, or 6 mL/kg, reduced if necessary to give a plateau airway pressure less than 30 cm H₂O. The trial was stopped early because the mortality rate was convincingly lower in the low tidal volume group (31.0 percent vs. 39.8 percent) (Figure 2, p. 10). This dramatic result led intensive care specialists to change immediately their goals of ventilation by adopting a low tidal volume strategy in ARDS patients. The 6 mL/kg tidal volume is now the standard of care for ARDS patients.

The University of Chicago Joins the ARDSNet
After this successful result, the ARDSNet hopes to answer more of the remaining important questions regarding care of ARDS patients. University of Chicago faculty in the Medical Intensive Care Unit have been selected to join the ARDSNet to study the role of fluid therapy and the pulmonary artery catheter. Many physicians judge a pulmonary artery catheter to be absolutely essential in the management of these critically ill patients. Yet no studies have shown any advantage to their use. Indeed, several investigators have reached the disturbing conclusion that pulmonary artery catheters may be contributing to harm. Some intensive care specialists have called for a moratorium on the use of the catheter. Over the next 2 years, patients with ARDS at ARDSNet hospitals will be randomized to receive either a pulmonary artery catheter or a simpler, central venous catheter. They will be randomized independently to be treated with a conservative fluid strategy, or a liberal approach. The primary outcome measure will be the rate of mortality at 60 days.

Critical Care at the University of Chicago
State-of-the-art care of ARDS patients at the University of Chicago is facilitated by a new Medical Intensive Care Unit that opened in January 2001. This 16-bed facility is staffed by highly trained intensive care unit nurses, respiratory therapists, and full-time pulmonary and critical care specialists. Highly sophisticated mechanical ventilators are used routinely. bedside monitors are networked to a central computer to allow storage and analysis of a wealth of clinical data from each patient. Our patients have access to a large number of clinical trials (including the ARDSNet study), which seek to define effective therapies and map out the future of critical care.

Conclusion
ARDS is a serious condition with a high mortality rate and no effective pharmacological therapy. The details of supportive therapy matter greatly, as is demonstrated by the lifesaving effect of low tidal volume ventilation in the ARDSNet trial. Such results support a recommendation that patients with ARDS be cared for in a center with extensive experience in the care of this complex condition. Many questions remain about the best supportive management. We are hopeful that the next series of studies will lead to even better care for patients with ARDS.

References