expressed as $V_A = V_E (1 – V_D/V_T)$. Normal physiologic dead space is ~150 mL (~2 mL/kg), making the V_D/V_T for a 500-mL tidal volume breath 0.3. In acute respiratory failure due to ARDS, for example, V_D may increase due to poorly perfused but ventilated portions of lung, while ventilation strategies lead to low V_T; thus, a modest increase in V_D to 200 mL and a low V_T of 300 mL will result in a V_D/V_T of 0.66, a situation where hypercapnia may easily develop. Hypercapnia in the context of low tidal volume (6 mL/kg) ventilation for ARDS often causes acute respiratory acidosis that can be managed with higher respiratory rates, up to 30 breaths/min. Respiratory acidosis is often tolerated down to a pH of 7.2, so-called “permissive hypercapnia,” but progressive acidosis may require intravenous alkalinizing therapy (e.g., sodium bicarbonate or tromethamine) or accepting an increase in V_T. In severe exacerbations of obstructive lung disease, COPD, and status asthmaticus, hypercapnia and acute respiratory acidosis are common despite mechanical ventilation, with average $Paco_2$ values of 65 mmHg and blood pH of 7.20 after initial endotracheal intubation. Poor alveolar ventilation is primarily due to dead space created by alveolar capillary compression in areas of alveolar overdistension and lung hyperinflation. Increasing minute ventilation by increasing the respiratory rate or tidal volume will, therefore, often paradoxically worsen hypercapnia by increasing gas trapping and V_D/V_T. The optimal ventilator strategy for severe obstructive lung disease physiology entails using lower respiratory rates, usually 9–12 breaths/min, and moderate tidal volumes (7–9 mL/kg) to maintain a minute ventilation of ~10 L/min; higher minute ventilation usually worsens hyperinflation and can cause barotrauma. To prevent dyspneic patients from driving hyperventilation, deeper sedation and occasionally neuromuscular blockade are necessary until severe bronchial obstruction responds to medical therapy. Although permissive hypercapnia can minimize barotrauma and volume trauma during mechanical ventilation, hypercapnia has adverse effects including increased intracranial pressure, pulmonary artery vasoconstriction, and even depressed cardiac contractility **(Table 302-3)**. The benefits and risks of a hypercapnia ventilatory strategy must, therefore, account for the individual patient’s comorbid medical