ARDS. Use of these agents may result in prolonged weakness—a myopathy known as the *postparalytic syndrome*. For this reason, neuromuscular blocking agents typically are used as a last resort when aggressive sedation fails to achieve patient-ventilator synchrony. Because neuromuscular blocking agents result in pharmacologic paralysis without altering mental status, sedative-induced amnesia is mandatory when these agents are administered.

Amnesia can be achieved reliably with benzodiazepines such as lorazepam and midazolam as well as the the IV anesthetic agent propofol. Outside the setting of pharmacologic paralysis, few data support the idea that amnesia is mandatory in all patients who require intubation and mechanical ventilation. Since many of these critically patients have impaired hepatic and renal function, sedatives and opiates may accumulate when given for prolonged periods. A nursing protocol–driven approach to sedation of mechanically ventilated patients or daily interruption of sedative infusions paired with daily spontaneous breathing trials has been shown to prevent excessive drug accumulation and shorten the duration of both mechanical ventilation and ICU stay.

MULTIORGAN SYSTEM FAILURE

Multiorgan system failure, which is commonly associated with critical illness, is defined by the simultaneous presence of physiologic dysfunction and/or failure of two or more organs. Typically, this syndrome occurs in the setting of severe sepsis, shock of any kind, severe inflammatory conditions such as pancreatitis, and trauma. The fact that multiorgan system failure occurs commonly in the ICU is a testament to our current ability to stabilize and support single-organ failure. The ability to support single-organ failure aggressively (e.g., by mechanical ventilation or by renal replacement therapy) has reduced rates of early mortality in critical illness. As a result, it is uncommon for critically ill patients to die in the initial stages of resuscitation. Instead, many patients succumb to critical illness later in the ICU stay, after the initial presenting problem has been stabilized.

Although there is debate regarding specific definitions of organ failure, several general principles governing the syndrome of multiorgan system failure apply. First, organ failure, no matter how it is defined, must persist beyond 24 h. Second, mortality risk increases with the accrual of failing organs. Third, the prognosis worsens with increased duration of organ failure. These observations remain true across various critical care settings (e.g., medical versus surgical). SIRS is a common basis for multiorgan system failure. Although infection is a common cause of SIRS, "sterile" triggers such as pancreatitis, trauma, and burns often are invoked to explain multiorgan system failure.

MONITORING IN THE ICU

Because respiratory failure and circulatory failure are common in critically ill patients, monitoring of the respiratory and cardiovascular systems is undertaken frequently. Evaluation of respiratory gas exchange is routine in critical illness. The "gold standard" remains arterial blood-gas analysis, in which pH, PaO_2, partial pressure of carbon dioxide (PCO_2), and O_2 saturation are measured directly. With arterial blood-gas analysis, the two main functions of the lung—oxygenation of arterial blood and elimination of CO_2—can be assessed directly. In fact, the blood pH, which has a profound effect on the drive to breathe, can be assessed only by such sampling. Although sampling of arterial blood is generally safe, it may be painful and cannot provide continuous information. In light of these limitations, noninvasive monitoring of respiratory function is often employed.

PULSE OXIMETRY

The most commonly utilized noninvasive technique for monitoring respiratory function, pulse oximetry takes advantage of differences in the absorptive properties of oxygenated and deoxygenated hemoglobin. At wavelengths of 660 nm, oxyhemoglobin reflects light more effectively than does deoxyhemoglobin, whereas the reverse is true in the infrared spectrum (940 nm). A pulse oximeter passes both wavelengths of light through a perfused digit such as a finger, and the relative intensity of light transmission at these two wavelengths is recorded. From this information, the relative percentage of oxyhemoglobin is derived. Since arterial pulsations produce phasic changes in the intensity of transmitted light, the pulse oximeter is designed to detect only light of alternating intensity. This feature allows distinction of arterial and venous blood O_2 saturations.

RESPIRATORY SYSTEM MECHANICS

Respiratory system mechanics can be measured in patients during mechanical ventilation (Chap. 323). When volume-controlled modes of mechanical ventilation are used, accompanying airway pressures can easily be measured as long as the patient is passive. The peak airway pressure is determined by two variables: airway resistance and respiratory system compliance. At the end of inspiration, inspiratory flow can be stopped transiently. This end-inspiratory pause (*plateau pressure*) is a static measurement, affected only by respiratory system compliance and not by airway resistance. Therefore, during volume-controlled ventilation, the difference between the peak (airway resistance + respiratory system compliance) and plateau (respiratory system compliance only) airway pressures provides a quantitative assessment of airway resistance. Accordingly, during volume-controlled ventilation, patients with increases in airway resistance typically have increased peak airway pressures as well as abnormally high gradients between peak and plateau airway pressures (typically >15 cmH_2O) at an inspiratory flow rate of 1 L/sec. The compliance of the respiratory system is defined by the change in pressure of the respiratory system per unit change in volume.

The respiratory system can be divided into two components: the lungs and the chest wall. Normally, respiratory system compliance is ~100 mL/cmH_2O. Pathophysiologic processes such as pleural effusions, pneumothorax, and increased abdominal girth all reduce chest wall compliance. Lung compliance may be reduced by pneumonia, pulmonary edema, interstitial lung disease, or auto-PEEP. Accordingly, patients with abnormalities in compliance of the respiratory system (lungs and/or chest wall) typically have elevated peak *and* plateau airway pressures but a normal gradient between these two pressures. Auto-PEEP occurs when there is insufficient time for emptying of alveoli before the next inspiratory cycle. Since the alveoli have not decompressed completely, alveolar pressure remains positive at the end of exhalation (*functional residual capacity*). This phenomenon results most commonly from critical narrowing of distal airways in disease processes such as asthma and COPD. Auto-PEEP with resulting alveolar overdistention may result in diminished lung compliance, reflected by abnormally increased plateau airway pressures. Modern mechanical ventilators allow breath-to-breath display of pressure and flow, permitting detection of problems such as patient-ventilator dyssynchrony, airflow obstruction, and auto-PEEP (Fig. 321–6).

CIRCULATORY STATUS

Oxygen delivery (Q_{O_2}) is a function of cardiac output and the content of O_2 in the arterial blood (Ca_{O_2}). The Ca_{O_2} is determined by the hemoglobin concentration, the arterial hemoglobin saturation, and dissolved O_2 not bound to hemoglobin. For normal adults:

$$\begin{aligned} Q_{O_2} &= 50\ \text{dL/min} \times (1.39 \times 15\ \text{g/dL [hemoglobin concentration]} \\ &\quad \times 1.0\ \text{[hemoglobin \% saturation]} + 0.0031 \times 100\ [Pa_{O_2}]) \\ &= 50\ \text{dL/min (cardiac output)} \times 21.6\ \text{mL } O_2\ \text{per dL blood } (Ca_{O_2}) \\ &= 1058\ \text{mL } O_2\ \text{per min} \end{aligned}$$

It is apparent that nearly all of the O_2 delivered to tissues is bound to hemoglobin and that the dissolved O_2 (Pa_{O_2}) contributes very little to O_2 content in arterial blood or to O_2 delivery. Normally, the content of O_2 in mixed venous blood ($C\bar{v}_{O_2}$) is 15.76 mL/dL since the mixed venous blood is 75% saturated. Therefore, the normal tissue extraction ratio for O_2 is $Ca_{O_2} - C\bar{v}_{O_2}/Ca_{O_2}$ ([21.16–15.76]/21.16) or ~25%. A pulmonary artery catheter allows measurements of O_2 delivery and the O_2 extraction ratio.

Information on the mixed venous O_2 saturation allows assessment of global tissue perfusion. A reduced mixed venous O_2 saturation may be caused by inadequate cardiac output, reduced hemoglobin concentration, and/or reduced arterial O_2 saturation. An abnormally high V_{O_2} may also lead to a reduced mixed venous O_2 saturation if O_2 delivery is