Chapter

41 CRITICAL CARE MEDICINE

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From the late 20th century to the present, critical care medicine has evolved as a dynamic, multidisciplinary field focused on the care of patients with life-threatening diseases. Anesthesia providers can play an important role in the care of the critically ill patient both in the operating room and intensive care unit (ICU). A few key topics in critical care with which the practicing anesthesia provider should be familiar include respiratory failure, shock, renal failure, and management of pain and sedation.

RESPIRATORY FAILURE

Respiratory failure remains a primary indication for admission to an ICU. The type of respiratory failure can be categorized based on the acuity of the process (e.g., acute vs. chronic) and the physiologic perturbation present (e.g., hypercapnia vs. hypoxemia). Such distinctions help to direct decision making for various treatment options. However, multiple processes can occur simultaneously. For example, a patient may have an acute and chronic respiratory failure with the presence of both hypoxemia and hypercapnia.

Hypoxemic respiratory failure generally occurs because of ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch leading to a large alveolar-arterial (A-a) gradient. Causes include trauma, acute respiratory distress syndrome (ARDS), sepsis, pneumonia, pulmonary embolism, cardiogenic pulmonary edema, and obstructive lung disease. Other physiologic causes of hypoxemia include intrapulmonary shunt, hypoventilation, and increased O_2 extraction (also see Chapter 5).

Causes of hypercapnic respiratory failure include hypoventilation, as may occur from a drug intoxication or

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Table 41.1 Different Settings of Mechanical Ventilation

Mode	Control	Limit	Cycle
AC	Volume	Volume	Volume
	Pressure	Pressure	Time
SIMV	Volume	Volume	Volume
	Pressure	Pressure	Time
PS		Pressure	Flow

AC, Assist control; *PS*, pressure support; *SIMV*, synchronized intermittent mandatory ventilation.

neuromuscular weakness, or increased dead space, which occurs with chronic obstructive pulmonary disease (COPD) or asthma. Hypercapnia may also be present in severe forms of an infiltrative pulmonary process, such as ARDS. Both hypercapnic and hypoxemic respiratory failure may require initiation of mechanical ventilator support.

Mechanical Ventilation

In modern ICUs, mechanical ventilation is performed entirely via positive-pressure ventilation. It may be accomplished through a noninvasive approach (via face mask or nasal mask) or an invasive approach (via endotracheal tube [ETT] or tracheostomy). The goals of mechanical ventilation include (1) decreasing the work of breathing; (2) improving oxygen delivery; (3) facilitating carbon dioxide removal; and (4) minimizing ventilator-associated lung injury. The settings for mechanical ventilation describe how the ventilator interacts with the patient (Table 41.1).

Modes

Assist Control

In assist control (AC) mode, the ventilator is set to deliver a minimum number of breaths per minute, while allowing the patient to initiate breaths as well. All mandatory and spontaneous breaths are fully supported to the same degree. So, if tidal volume is set at 500 mL, then all breaths (i.e., mandatory and spontaneous) will receive a tidal volume of 500 mL.

Synchronized Intermittent Mandatory Ventilation

With synchronized intermittent mandatory ventilation (SIMV), the ventilator attempts to synchronize the mandatory mechanical breaths with the patient's spontaneous breaths in order to decrease ventilator dyssynchrony. If there are no spontaneous breaths within the preset time interval, then the ventilator will deliver the mandatory breath. The breaths in between the mandatory breaths are not fully supported, unlike the AC mode. For these nonmandatory breaths, the ventilator can be set to deliver pressure support (PS), as described next.

Pressure Support

PS mode is used only with spontaneously breathing patients, as all breaths are triggered by patient effort. The driving pressure (ΔP), positive end-expiratory pressure (PEEP), and fraction of inspired oxygen (F_{IO_2}) are the only variables set in this mode. Inspiratory flows are based on patient demand. The ventilator ends inspiration when the flow rate has decreased to a predetermined level (usually 25% of the peak flow rate). There is no backup respiratory rate in PS mode unless it is combined with SIMV.

Other Modes

The sophisticated microprocessors in current ventilators enable novel modes such as adaptive support ventilation, airway pressure release ventilation, and proportional assist ventilation. These modes offer potential physiologic benefits but have not been subject to large clinical trials with enough power to demonstrate improved mortality rate.

Limits

With AC or SIMV mode, the limit or control needs to be specified. With volume control (VC), a preset tidal volume is delivered during inspiration. With pressure control (PC), a preset inspiratory pressure is delivered by the ventilator.

Volume Control

Sample mechanical ventilation orders for AC and SIMV with VC are listed in Table 41.2. The tidal volume, rate, PEEP, and F_{IO_2} must be specified. The inspiratory flow rate is not typically part of a standard ventilator order set and is set by the respiratory therapist. A typical inspiratory flow rate is 60 L/min. By increasing inspiratory flow, the set tidal volume is delivered in a shorter time, which allows more time for exhalation. This strategy may be beneficial for an asthmatic patient in respiratory distress to increase expiratory time. The flow waveform in VC can be decelerating or constant (so-called square wave).

Pressure Control

In AC or SIMV mode with PC, a driving pressure must be specified. Additionally, an inspiratory time or inspiratory-expiratory time (I:E) ratio is set. The peak flows in PC are variable and based on demand. By default, the flow waveform must be decelerating in order to maintain a constant peak inspiratory pressure. Tidal volumes are not guaranteed and if lung compliance changes quickly, vigilance is necessary to make sure minute ventilation does not drop rapidly.

Dual Control

The choice between VC or PC is not supported by definitive evidence. Modern ventilators can combine the features of both, targeting specified tidal volumes, but delivering each breath in a PC mode with decelerating flows. If pulmonary compliance changes, then the ventilator automatically adjusts the pressure gradually over a few breaths to maintain the targeted tidal volumes. Many

Table 41.2 Sample Orders for Mechanical Ventilation

Example	Ventilator Orders Written	Additional Settings That Can Be Ordered	Explanation
Example 1: Assist control–volume control (AC-VC)	Mode AC/VC Rate 10 V_T 500 mL PEEP 5 cm H_2O F_{IO_2} 1.0	Flow rate: typically 60 L/min Trigger: flow or pressure	Ventilator will deliver the preset tidal volume of 500 mL 10 times a minute; if the patient's respiratory rate is greater than 10, each breath will also be 500 mL
Example 2: Assist control–pressure control (AC-PC)	Mode AC/PC Rate 10 PIP 20 cm H_2O PEEP 5 cm H_2O F_{IO_2} 1.0	I:E ratio: typically 1:2 Inspiratory time Trigger: flow or pressure	Ventilator will deliver 10 breaths per minute; each breath will reach a peak pressure of 20 cm H_2O; if the patient's respiratory rate is greater than 10, each breath will also reach peak pressure of 20 cm H_2O
Example 3: Synchronized intermittent mandatory ventilation–volume control (SIMV-VC)	Mode SIMV-VC Rate 10 V_T 500 mL Pressure support 5 cm H_2O PEEP 5 cm H_2O F_{IO_2} 0.5	Flow rate: typically 60 L/min Trigger: flow or pressure (this applies to all the breaths, SIMV, or pressure support)	Ventilator will deliver 10 breaths per minute with tidal volume 500 mL; if the patient's respiratory rate is greater than 10, those nonmandatory breaths will receive inspiratory pressure support to peak pressure 5 cm H_2O above the PEEP of 5 cm H_2O
Example 4: Pressure support ventilation (PSV)	Mode PSV Driving pressure 8 cm H_2O PEEP 5 cm H_2O F_{IO_2} 0.5	Trigger: flow or pressure	Patient must be breathing spontaneously; each breath will receive inspiratory pressure support to peak pressure 8 cm H_2O above the PEEP of 5 cm H_2O

F_{IO_2}, Fraction of inspired oxygen; *I:E*, inspiratory to expiratory ratio; *PEEP*, positive end-expiratory pressure; *PIP*, peak inspiratory pressure; *V_T*, tidal volume.

proprietary names exist, such as *pressure control ventilation-volume guaranteed, pressure-regulated volume control,* or *volume control plus.*

Cycle

The cycle determines how the ventilator switches from inspiration to expiration. For AC-VC or SIMV-VC modes, volume determines the ventilator cycle. Inspiration is complete when the tidal volume is delivered (see Table 41.1). For AC-PC or SIMV-PC, inspiration is complete when the inspiratory time has ended. With PS mode, a decrease in the inspiratory flow rate determines the end of the inspiratory cycle. Knowledge of how the ventilator cycles can allow better understanding of patient/ventilator dyssynchrony. For example, a patient in respiratory distress receiving mechanical ventilation in the AC-VC mode may find the set tidal volume too small and "double stack" (i.e., take a second breath during the start of the ventilator's exhalation phase). Or, a patient receiving AC-PC ventilation may begin exhalation prior to the end of the set inspiratory time.

Other Settings

Positive End-Expiratory Pressure

PEEP is constant positive airway pressure that is applied throughout the respiratory cycle. PEEP is generated by a pressure relief valve on the expiratory limb of the ventilator circuit. The use of PEEP leads to an increased mean airway pressure, which decreases atelectasis and improves oxygenation. PEEP also increases functional residual capacity and can improve pulmonary compliance.

If PEEP is too large, alveolar overdistention can occur, which may lead to barotrauma. Excessive PEEP can also reduce preload and cause hypotension. Auto-PEEP occurs when a buildup of end-expiratory pressure results from insufficient exhalation time. Emergent treatment of auto-PEEP entails disconnecting the patient from the ventilator to release the PEEP. Treatment of auto-PEEP requires increasing expiratory time (i.e., changing the ratio of the duration of inspiration to the duration of expiration, or I:E ratio).

Trigger

The trigger refers to the manner by which the ventilator detects patient inspiration and delivers positive pressure in synchrony with the patient's efforts. The trigger variable, which can be based on flow or pressure, is not part of a typical ventilator order set and is often managed by respiratory therapists. Usual triggers are a change in flow of 2 L/min or a change in pressure of 2 cm H_2O. Smaller or larger triggers can be set based on the clinical situation.

For example, patients with bronchopleural fistulas may constantly trigger mechanical ventilation breaths if the flow trigger is too sensitive.

Noninvasive Positive-Pressure Ventilation

Noninvasive positive-pressure ventilation (NIPPV) delivers positive-pressure breaths via a face mask, nasal pillows, or helmet without an ETT present. For patients with COPD and acute hypercapnic respiratory failure (AHRF), appropriate use of NIPPV can reduce mortality rate, avoid endotracheal intubation, improve dyspnea, and reduce hospital length of stay. Other established indications for NIPPV include acute cardiogenic pulmonary edema, postoperative respiratory failure, and hypoxic respiratory failure in immunocompromised patients (e.g., organ and bone marrow transplant recipients).

The data for NIPPV are often impressive, but the patients chosen for these studies were judiciously selected in trials with close clinical observation. NIPPV is most beneficial in patients who have a potentially rapidly reversible pulmonary process that requires some ventilator support. Delays in endotracheal intubation can lead to an emergent event that is more prone to complications. Contraindications for using NIPPV are listed in Box 41.1. The most commonly used ventilator mode for NIPPV is PS.

High-Flow Nasal Cannula

Use of high-flow nasal cannula (HFNC) has emerged as an alternative to NIPPV. HFNC uses heated and humidified oxygen that is delivered at high flow rates through nasal cannula. This delivery system provides a small amount of positive airway pressure and reduces dead space by flushing expired carbon dioxide from the upper airways. Most patients find HFNC to be more comfortable and easier to tolerate than NIPPV via a face mask. A 2015 multicenter trial in patients with acute hypoxemic, nonhypercarbic respiratory failure showed that high-flow oxygen therapy, as compared with standard oxygen therapy or noninvasive ventilation, resulted in reduced mortality rate in the ICU and at 90 days, although there was no difference in the rate of tracheal intubation.[1]

Box 41.1 Contraindications for Noninvasive Positive-Pressure Ventilation

- Impaired neurologic state (coma, seizures, encephalopathy)
- Respiratory arrest or upper airway obstruction
- Shock or severe cardiovascular instability
- Severe upper gastrointestinal bleeding
- Recent gastroesophageal surgery
- Vomiting
- Excessive airway secretions
- Facial lesions that prevent proper fit of nasal or facial masks

Weaning From Mechanical Ventilation and Tracheal Extubation

Weaning may account for more than 40% of the patient's time on mechanical ventilation depending on the definition of when weaning commences. To decrease the risk of ventilator-associated pneumonia (VAP), patients should be weaned from mechanical ventilation as soon as they have recovered from the process that originally required mechanical ventilator support.

The average rate of failed tracheal extubation (i.e., inadequate ventilation following extubation of the trachea) in surgical ICUs is 5% to 8%, whereas in medical and neurologic ICUs the rate is 17%. Although many criteria are listed in the following section, no one algorithm can accurately predict successful tracheal extubation. A cautiously applied aggressive approach to weaning from mechanical ventilation and tracheal extubation results in fewer ICU-related complications, although definitive data from randomized trials are lacking.

Criteria for Weaning Trial

A-a Gradient

The patient should have adequate oxygenation, usually defined as $Pa_{O_2}/F_{I_{O_2}}$ more than 150 mm Hg with PEEP less than 8 cm H_2O. This amount of oxygen is chosen because this level can be reliably delivered via face mask or nasal cannula. An oxygen requirement greater than this denotes that the patient still has a large shunt fraction and the underlying pulmonary process may not have resolved adequately. In the end, these criteria are just guidelines. The final decision regarding what is an appropriate A-a gradient is often based on clinical judgment and experience.

Respiratory Mechanics

Rapid Shallow Breathing Index

Rapid shallow breathing index (RSBI) is the ratio of respiratory rate (breaths/min) to tidal volume (in liters). This index is the most extensively studied and commonly used weaning predictor. A RSBI less than 105 breaths/min/L (i.e., positive RSBI) is associated with weaning success, but a negative RSBI (RSBI more than 105 breaths/min/L) is likely better at identifying patients who will fail than a positive RSBI is at identifying patients who can succeed.

Maximum Inspiratory Force

Patients must have the respiratory muscle strength to generate an adequate tidal volume. One attempt to measure this is via the maximum inspiratory force (MIF). For weaning, a MIF of at least −20 cm H_2O is preferable. A normal MIF indicates little or no increase in the probability of weaning success, but a small MIF predicts a small increase in the probability of weaning failure. One reason for the poor predictive ability of the MIF is the challenge of obtaining an accurate measurement in a spontaneously breathing patient. In many ICUs, MIF is not routinely

measured prior to weaning from ventilation. However, if a patient is not progressing in the weaning process, measurement of a MIF may suggest a cause such as muscle weakness or deconditioning.

Other Criteria

Other respiratory criteria may impact success of weaning from ventilation, including the nature and amount of airway secretions and the ability to clear secretions, which involves the gag reflex and cough strength. The presence of upper airway edema may promote airway obstruction and hypoxemia after tracheal extubation. The cuff leak test is one method to assess for airway edema. The ETT cuff is deflated and positive pressure is delivered through the ETT until an air leak is heard. A leak pressure of less than 10 cm H_2O suggests the absence of airway edema. In contrast, a leak pressure greater than 20 cm H_2O may indicate significant airway edema and should be considered prior to the decision for tracheal extubation.

Other patient factors that impact weaning include mental status and hemodynamics. Patients should have an adequate level of consciousness to protect their airway from aspiration of gastric contents. In addition, patients should be hemodynamically stable, because discontinuation of positive-pressure ventilation can lead to increased work of breathing and alter left ventricular preload and afterload.

Weaning Strategies

Regardless of the weaning strategy used in ICUs, early identification of patients who are able to breathe spontaneously results in better outcomes. A common strategy is for the mechanically ventilated patient to undergo a daily assessment of readiness.[2] If the patient is deemed ready, a spontaneous breathing trial (SBT) is performed. If the factors described previously (respiratory mechanics, mental status, hemodynamics) remain adequate throughout the SBT, a decision for tracheal extubation can be made. Protocol-based weaning by nurses and respiratory therapists allows more rapid tracheal extubation compared to physician-directed weaning.

The SBT can be conducted with different ventilation modes, including PS ventilation or T-piece trial. There is no definitive evidence of a superior mode associated with more frequent weaning success, less need for tracheal reintubation, or lower ICU fatality.[3] However, for an individual patient, a specific mode may have clinical advantages. For example, in patients with heart failure and reduced cardiac ejection fraction, the change from positive-pressure ventilation to negative-pressure ventilation can increase left ventricular afterload and worsen cardiovascular strain. This patient may benefit from T-piece trial for the SBT, because even low levels of positive pressure and PEEP may provide afterload reduction. If the patient does not develop signs of pulmonary edema during the T-piece trial, the decision for tracheal extubation can proceed.

The optimal duration of an SBT is unknown, but most range from 30 minutes to 2 hours. Longer periods may be required for patients with chronic respiratory failure whose tracheas have been intubated for an extended duration or for patients who fail their initial SBT. In select patients, weaning strategies that include NIPPV can reduce the rate of mortality, VAP, and weaning failure without increasing the risk of tracheal reintubation.[4] This approach may be considered in patients who do not have difficult to manage airways, excessive secretions, or an impaired mental status and should be coupled with an early decision regarding tracheal reintubation if the patient remains tachypneic or in distress. Tracheal reintubation, especially if delayed, is associated with increased mortality rate, longer hospital stay, and lower likelihood of returning home.

Automated closed-loop systems (e.g., SmartCare/PS, adaptive support ventilation, proportional assist ventilation, volume support ventilation) were developed to adapt ventilation in response to real-time changes with the patient's respiratory mechanics. A recent meta-analysis showed that closed-loop systems reduced the duration of ventilation and ICU length of stay in mixed (combined medical-surgical ICUs) or medical ICU patients; however, more randomized controlled trials are needed for surgical ICU patients and patients using other automated systems.[5] Currently, this area of research is in its infancy.

Acute Respiratory Distress Syndrome

ARDS, characterized as a diffuse, inflammatory injury of the lung, results in the development of noncardiogenic pulmonary edema with resultant $\dot{V}/\dot{Q}$ mismatch, hypoxemia, and decreased pulmonary compliance. ARDS typically follows an inciting event that can lead to direct or indirect lung injury (Table 41.3). Although the underlying cause of lung injury may predict outcome, patient-specific factors such as age, immunocompromised status, and organ dysfunction are stronger predictors for survival. In

Table 41.3 Causes of Acute Respiratory Distress Syndrome

Causes of Direct Lung Injury	Causes of Indirect Lung Injury
Pneumonia	Sepsis
Aspiration of stomach contents	Severe trauma
Pulmonary contusion	Cardiopulmonary bypass
Reperfusion pulmonary edema	Drug overdose
Amniotic fluid embolus	Acute pancreatitis
Inhalational injury	Near-drowning, transfusion-related acute lung injury

Data from Ware LB, Matthay MA. The acute respiratory distress syndrome. *N Engl J Med*. 2000;342:1334-1349.

Table 41.4 Comparison of the American-European Consensus Conference and Berlin Definition of Adult Respiratory Distress Syndrome

	AECC Definition	Berlin Definition
Timing	Acute onset	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Oxygenation	**ALI**: $PaO_2/FiO_2 \leq$ 300 mm Hg **ARDS**: $PaO_2/FiO_2 \leq$ 200 mm Hg	**Mild**: 200 mm Hg < $PaO_2/FiO_2 \leq$ 300 mm Hg with PEEP or CPAP ≥ 5 cmH_2O **Moderate**: 100 mm Hg < $PaO_2/FiO_2 \leq$ 200 mm Hg with PEEP ≥ 5 cmH_2O **Severe**: $PaO_2/FiO_2 \leq$ 100 mm Hg with PEEP ≥ 5 cmH_2O
Chest radiograph	Bilateral infiltrates	Bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules
Edema	PAWP ≤ 18 mm Hg when measured or no clinical evidence of left atrial hypertension	Respiratory failure not fully explained by cardiac failure or fluid overload
Risk factor	Not included in definition	If no risk factor for lung injury identified, then need objective assessment such as echocardiography to exclude hydrostatic edema

AECC, American-European consensus Conference; *ALI*, acute lung injury; *ARDS*, acute respiratory distress syndrome; *FiO_2*, fraction of inspired oxygen; *PaO_2*, arterial partial pressure of oxygen; *PAWP*, pulmonary artery wedge pressure; *PEEP*, positive end-expiratory pressure.
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some patients, ARDS resolves following an acute phase but others experience a chronic alveolitis leading to pulmonary fibrosis. Such patients often experience continued hypoxemia, increased physiologic dead space, and decreased compliance with chronic ventilator dependence.

Although classically defined by an increased A-a gradient in the setting of diffuse bilateral noncardiogenic pulmonary infiltrates, the clinical definition of ARDS continues to evolve—most recently with the Berlin criteria (Table 41.4).[6] In this new definition, the clinical distinction between ARDS and acute lung injury disappears and is replaced by categories of severity (i.e., mild, moderate, and severe). Additionally, the requirement for pulmonary artery occlusion pressure (PAOP) measurement no longer exists. In the absence of a known cardiac event, objective data such as echocardiography are required to rule out cardiogenic pulmonary edema as the cause of bilateral infiltrates.

Management

Because many clinical trials of pharmacologic immune modulation have shown no benefit, treatment for ARDS remains largely supportive, with a focus on the prevention of further lung injury. The central tenet for ARDS care involves lung protective ventilation when mechanical ventilation is required. In the landmark ARDS Network (ARDSnet) trial, "lower tidal volume (6 mL/kg of ideal body weight)" ventilation reduced mortality rate (31% vs. 40%) as compared to standard ventilation practices (12 mL/kg).[7] The theory is that by accepting decreased Po_2 and increased Pco_2 values ("permissive" hypoxemia and hypercapnia), the avoidance of large tidal volumes and high airway pressures decreases the incidence of barotrauma and volutrauma, and mortality rate.

Physician-directed lung protective ventilation protocols allow respiratory therapists to proactively adjust ventilator settings to maintain lung protective criteria. A lower threshold should be used to initiate lung protective ventilation, as patients who are ventilated with lung protective protocols and who are later ruled out for ARDS suffer no worse clinical outcomes.[8] Furthermore, intraoperative lower tidal volume ventilation may reduce the risk for developing ARDS postoperatively.

Patients with moderate to severe ARDS may benefit from administration of neuromuscular blocking drugs (NMBDs) (also see Chapter 11). NMBDs often improve pulmonary compliance and oxygenation. A clinical trial of early cisatracurium infusion in ARDS patients demonstrated improved 90-day survival rate although the mechanism for the benefit is not clear.[9] The prone position may improve oxygenation and clinical outcomes and should be used in the management of severe ARDS. However, a medical facility's experience and comfort in caring for critically ill patients while prone should be considered prior to initiating this procedure. Finally, referral for extracorporeal life support (ECLS) may be indicated, although data for improved outcomes do not currently exist. Clinical trials are being conducted to explore this resource intensive therapy.

Tracheostomies

A small, but significant portion of patients may require prolonged mechanical ventilation during their critical illness. Tracheostomies often facilitate rehabilitation and allow for weaning of sedation. However, the timing of tracheostomies remains a controversial topic. Early tracheostomies (≤4 days) do not decrease 30-day mortality rate, 2-year mortality rate, or ICU length of stay in patients when compared to those who received late tracheostomies (≥10 days).[10] Physicians are poor at predicting those patients requiring prolonged mechanical ventilation. Only 45% of the patients who were predicted to require more

Table 41.5 Characteristics of Various Shock States

Shock Type	Cardiac Output	Systemic Vascular Resistance	Central Venous Pressure	Pulmonary Capillary Wedge Pressure	Mixed Venous Oxygen Saturation
Hypovolemic	↓	↑	↓	↓	↓
Cardiogenic	↓	↑	↑	↑[a]	↓
Vasodilatory	↑ or ↔	↓	↓	↓	↑ or ↔

[a]Pulmonary capillary wedge pressure is normal to low in right ventricular failure.

than 7 days of mechanical ventilation actually required a tracheostomy. The remaining 55% were successfully extubated. Because of this, with the exception of certain clinical situations, tracheostomies are often deferred until 10 to 14 days after tracheal intubation. Placement of tracheostomies can lead to the loss of mean airway pressure and derecruitment of alveolar units, so tracheostomies should be deferred in unstable patients and those with high PEEP and oxygen requirements.

Inadvertent dislodgement of the tracheostomy tube during the first 7 days after placement is a potentially life-threatening problem. In this circumstance, blind tracheostomy tube advancement may result in tube passage through a false subcutaneous track rather than into the trachea. When feasible, orotracheal intubation should be the first maneuver to obtain a secure airway. Otherwise, a pediatric laryngoscope blade may be inserted into the stoma and a new tracheostomy tube or ETT can be inserted under direct visual identification of tracheal rings.

SHOCK

Shock is a common clinical condition encountered in critically ill patients. Many clinical processes can cause shock that leads to inadequate perfusion to major organ systems, such as the brain, heart, kidney, liver, and abdominal viscera. This in turn leads to anaerobic metabolism, multiorgan failure, and death when adequate perfusion cannot be restored. Shock is categorized by the underlying physiologic process that induced the state of hypoperfusion. Major categories include hypovolemic, cardiogenic, and vasodilatory shock. Vasodilatory shock can be further categorized as septic, anaphylactic, and neurogenic shock. Characteristics of the major categories of shock are listed in Table 41.5.

Hypovolemic Shock

Hypovolemic shock occurs following an acute, decompensated decrease in circulating blood volume (also see Chapters 42 and 45. Decreases in intravascular volume reduce cardiac preload (left ventricular end-diastolic volume), which is a major determinant of cardiac output. Hypovolemia most commonly occurs during massive blood loss from trauma, surgery, or gastrointestinal hemorrhage (also see Chapter 24). When compensatory mechanisms are unable to restore adequate perfusion of the vital organs, shock and hemodynamic collapse result.

Clinical Manifestations

Acute blood loss initially results in the translocation of interstitial fluid into the circulating blood volume to transiently restore cardiac output. This response helps to explain some of the physical examination findings found in patients with hypovolemic shock, including dry mucous membranes and decreased skin turgor. Following this fluid shift, activation of the renin-angiotensin-aldosterone system results in sodium conservation by the kidneys and restoration of interstitial fluid loss.

If cardiac output continues to decrease from inadequate circulating blood volume (>15% reduction), the baroreceptor reflex triggers an increase in the heart rate to maintain cardiac output. Sympathetic stimulation through the release of endogenous catecholamines from the adrenal glands produces vasoconstriction of nonessential organs. Blood is redirected away from the skin, skeletal muscle, and the splanchnic circulation to maintain perfusion of vital organs. Patients may appear cold, clammy, and vasoconstricted. Mesenteric ischemia may result if the condition persists. If circulating volume loss continues (>40% reduction) in the absence of adequate resuscitation, compensatory mechanisms may no longer be able to maintain cardiac output and decompensated hypovolemic shock follows.

Treatment

Adequate intravascular volume resuscitation and source control are key to the treatment of hypovolemic shock. First, adequate intravenous access must be obtained quickly. Ideal access involves short, large-bore intravenous peripheral catheters, preferably 16-gauge or greater. Central access should be reserved for patients for whom large-bore peripheral access cannot be obtained. If intravenous access cannot be readily obtained, an intraosseous (IO) catheter can be placed to allow for the initiation of resuscitation (also see Chapter 24). Fluids, blood products, and vasopressors may be administered through this line. IO access should be exchanged for intravenous access once the patient has been stabilized because of concerns about compartment syndrome from extravasation or osteomyelitis from prolonged needle placement.

In patients with mild to moderate intravascular volume loss, cardiovascular resuscitation may begin with the intravenous administration of isotonic fluids. Balanced salt solutions, such as lactated Ringer solution or Plasma-Lyte, may be preferable, as their composition and osmolality more closely resemble that of human plasma. If vital signs improve in response to resuscitation, then laboratory measurements (especially hemoglobin values) may be obtained to guide the need for blood products (also see Chapter 24). In trauma patients (also see Chapter 42), permissive hypotension may need to be employed until bleeding is controlled in patients requiring emergent surgical intervention.

In the event of moderate to severe hypovolemic shock because of acute blood loss, the empiric administration of blood products may be necessary prior to obtaining laboratory measurements. Additionally, an initial hematocrit value may be misleading if compensatory mechanisms or crystalloid resuscitation has not led to the dilution of the remaining red blood cell mass. During massive transfusion, defined as the need for 10 units packed red blood cells in 24 hours or 4 units in 1 hour, fresh frozen plasma and platelets should be administered in a 1:1:1 ratio to packed red blood cells[11] (also see Chapter 24).

Cardiogenic Shock

Cardiogenic shock results when either the left or right ventricle is unable to contract efficiently to generate an adequate stroke volume. Ventricular end-diastolic volume rises leading to distention of the ventricle and the development of pulmonary edema in left-sided failure or distended neck veins, peripheral edema, and hepatic congestion in right-sided failure. Biventricular failure can result when the pulmonary congestion from left ventricular failure leads to pulmonary artery hypertension and concomitant right ventricular failure.

Clinical Manifestations

Causes of cardiogenic shock include acute myocardial infarction, severe cardiomyopathy, myocarditis, arrhythmia, valvular rupture, or ventricular septal defect. A decreased stroke volume reduces cardiac output and arterial blood pressure. To maintain systolic blood pressure, compensatory tachycardia occurs to offset the decreased stroke volume. This often worsens myocardial oxygen balance as the tachycardia increases oxygen consumption by allowing less time for diastolic subendocardial perfusion. Increasing end-diastolic pressure further reduces subendocardial blood flow, worsening oxygen delivery to the failing ventricle. As ventricular function continues to fail, the compensatory tachycardia is unable to maintain cardiac output and hypotension follows. Patients often develop poorly perfused extremities as sympathetic outflow leads to peripheral vasoconstriction.

Treatment

Pharmacologic interventions aim to improve cardiac output, cardiac filling pressures, and myocardial oxygen balance. Invasive monitors, including arterial and central venous lines, help to guide therapy. PAOP measurements may be indicated, but the risks and benefits of pulmonary artery line placement must be carefully considered. In severe cardiogenic shock with hypotension, the administration of inotropic and vasopressor support helps to increase perfusion to the myocardium and other vital organs, but may increase myocardial oxygen demand. For severe hypotension, administration of norepinephrine as compared to dopamine improves outcomes with fewer arrhythmias.[12]

When hypotension is absent, dobutamine should be given to provide inotropic support. As an inodilator, dobutamine often decreases arterial blood pressure but improves forward flow and perfusion of vital organs. Often norepinephrine and dobutamine are administered in combination to improve cardiac output while maintaining adequate coronary artery filling pressures. Diuresis is key to improving cardiac filling pressures but should be undertaken judiciously if the hemodynamics are tenuous. In patients with evidence of cardiogenic shock accompanied by hypertension, vasodilators such as nitroprusside or nitroglycerin may help to decrease afterload and preload and improve forward flow.

Reversible causes of cardiogenic shock should be identified and addressed. For patients with cardiogenic shock complicating an acute myocardial infarction, early revascularization improves mortality rate.[13] Angiography with stenting is preferred when this procedure can be accomplished within 90 minutes. Otherwise, fibrinolytic therapy should be considered when not contraindicated. In the case of tachyarrhythmias precipitating cardiogenic shock, the preferred antiarrhythmic is amiodarone as it possesses less negative inotropic affects than β-adrenergic blockers or calcium channel blockers.

For selected patients with severe heart failure (i.e., left ventricular ejection fraction < 25% and hemodynamic compromise), mechanical support (i.e., intra-aortic balloon pump, extracorporeal membrane oxygenator, or left ventricular assist device) is a treatment option.

Vasodilatory Shock

Vasodilatory shock encompasses an array of well-defined clinical entities that include septic, anaphylactic, and neurogenic shock. Vasodilatory shock results from profound dilation of the arterial vascular system leading to decreased systemic vascular resistance (SVR) and hypotension. Capillary leakage of intravascular volume into the extracellular space further worsens the hemodynamics and leads to tissue hypoperfusion, which results in anaerobic metabolism and lactic acidosis. Tachycardia

and increased stroke volume attempt to compensate for the decrease in SVR to restore arterial blood pressure. If the underlying process continues to evolve, multiorgan ischemia and failure develop.

Clinical Manifestations

Vasodilation occurs via different mechanisms in septic, anaphylactic, and neurogenic shock. Septic shock occurs because of release of cytokines and an inflammatory response. Anaphylaxis is due to release of mediators from white blood cells triggered by immunologic mechanisms. Neurogenic shock generally follows a traumatic injury to the brain or spinal cord in which sympathetic outflow to the periphery is interrupted. The pooling of blood in vascular beds from low SVR leads to hypotension and circulatory failure. In early vasodilatory shock, patients may present with warm extremities. However, with disease progression, the skin can become cool and cyanotic as a result of poor end-organ perfusion.

Treatment

Treatment first involves replacement of the effective circulatory volume initially lost owing to pooling of venous blood or capillary leakage. When resuscitation of intravascular volume is unable to restore circulation, vasopressors should be given.

For septic shock, norepinephrine is considered the vasopressor of choice. Norepinephrine helps to restore SVR and arterial blood pressure through its α_1-adrenergic effects, while also providing cardiac support through its β_1-adrenergic effects. When compared to dopamine, norepinephrine results in fewer arrhythmias. When norepinephrine alone is not adequate to restore arterial blood pressure, epinephrine or vasopressin can be added. Epinephrine can also substitute for norepinephrine, but vasopressin is not recommended as the single initial vasopressor, and doses larger than 0.03 to 0.04 units/min should be reserved for salvage therapy.

In neurogenic shock, adequate perfusion to the injured spinal cord must be maintained to limit secondary ischemic injury, so the goal is to institute early appropriate fluid resuscitation. If there is an inadequate response to intravascular fluid resuscitation, vasopressors with α- and β-adrenergic activity should be initiated to counter the loss of sympathetic tone and provide chronotropic cardiac support if bradycardia is present.

Anaphylactic shock is treated initially with epinephrine as the vasopressor of choice. Epinephrine helps alleviate the bronchospasm that accompanies severe anaphylaxis, through its β_2-adrenergic effects, while also increasing SVR, stroke volume, and heart rate. Secondary treatments for anaphylaxis (i.e., histamine H_1 and H_2 blockers, bronchodilators, and glucocorticoids) do not prevent airway edema, hypotension, or shock and should not delay the administration of epinephrine.

Hemodynamic Monitoring

Appropriate monitoring of patients with shock plays a key role in treatment. Intensive care settings not only allow for more frequent monitoring but also for the placement of continuous, invasive monitors (i.e., arterial, central, and pulmonary artery catheters [PACs]).

Arterial Pressure

Arterial catheters are the most commonly inserted invasive monitors in the ICU. Besides obtaining minute-to-minute information regarding arterial blood pressure, arterial waveform analysis has gained acceptance as a tool to predict a patient's hemodynamic response to intravascular volume expansion. Chapter 20 describes variables derived from the arterial line, including systolic pressure variation (SPV) and pulse pressure variation (PPV). PPV is more accurate than cardiac filling pressures (central venous pressure [CVP], PAOP) to predict intravascular fluid responsiveness.

Central Venous Pressure

CVP monitoring, generally recorded at the junction of the superior vena cava and the right atrium, traditionally guided fluid therapy. However, CVP is a poor predictor of fluid responsiveness[14] (also see Chapter 20). Given their risks, central venous catheters should rarely be placed solely for measurement of CVP.

Pulmonary Artery Catheter

In the ICU, PAC use has associated insertion risks and lack of documented benefit. Randomized controlled trials in patients with ARDS were unable to demonstrate improved outcomes with the use of PACs as compared to CVP catheters. Clinical care has shifted more toward the use of noninvasive hemodynamic monitoring that offers dynamic measures of intravascular fluid responsiveness.

Bedside Ultrasonography

The use of bedside ultrasonography (including echocardiography) has increased in the ICU because of its ability to provide rapid information to aid in clinical diagnosis and management. The goal is to perform a focused examination to answer a specific clinical question.

With training in focused point-of-care echocardiography, critical care physicians are able to correctly identify ventricular dysfunction more than 80% of the time. The limitation of echocardiography is that it cannot provide continuous monitoring, but it can offer additional information such as valvular or pericardial anatomy.

In terms of fluid management, ultrasonography evaluation of the inferior vena cava (IVC) offers a noninvasive method to assess fluid responsiveness in patients who are mechanically ventilated. IVC size alone can be an indicator of volume status but not volume responsiveness (improved cardiac output after fluid challenge). IVC diameter variation (>15%) with positive-pressure

ventilation has correlated well with volume responsiveness. However, measurements should be taken during positive-pressure ventilation, the tidal volume should be at least 8 mL/kg, and the heart should be in sinus rhythm. Measurements taken during spontaneous respiration are less reliable because of variability in tidal volume and degree of IVC collapse.

Bedside ultrasonography can also provide procedural guidance for placement of peripheral intravenous catheters, arterial lines, and central venous catheters. Use of real-time ultrasound for internal jugular central line placement has been associated with fewer complications, fewer failed attempts, and shorter procedure times. There are fewer studies of ultrasound guidance for placement of arterial lines or subclavian central lines, but use of ultrasonography may improve the success rates of those procedures as well.

Ultrasonography can also help identify many pulmonary diseases in the ICU such as pleural effusion, pulmonary edema, pneumonia, and pneumothorax. For example, when alveoli are filled with fluid, reverberation artifacts can be seen on the pleural surface, which are called "B-lines" or "lung rockets." Identification of these B-lines indicates airspace disease, consistent with the diagnosis of ARDS, pulmonary edema, or pneumonia.

Sepsis

Sepsis is the leading cause of death in the ICU and is the most common reason for admission to the ICU. Patients with septic shock suffer an overwhelming systemic inflammatory response, which often ends in multiple organ dysfunction syndrome (MODS) and death. Many approaches have been proposed and negated over the past 10 years (e.g., activated protein C, tight glucose control, and use of glucocorticoids). However, the fundamental approach of early recognition, rapid cardiorespiratory resuscitation, immediate antibiotic administration, and identification and treatment of the infectious source has withstood the test of time.

The 2001 clinical trial of early goal-directed therapy (EGDT) in sepsis was based on (1) intravascular fluid resuscitation, (2) vasopressors to achieve a mean arterial pressure goal, and (3) packed red blood cell transfusion or dobutamine infusion to improve central venous oxygen saturation. The entire protocol-based algorithm occurred in the emergency department for 6 hours prior to ICU transfer.[15] The trial was monumental because the protocol group had improved clinical outcomes (shorter length of hospitalization and lower mortality rate). Subsequently, the algorithm was integrated into many ICU sepsis treatment bundles. However, three multicenter randomized controlled trials were recently published comparing EGDT with usual care or protocol-based standard care.[16-18] All three trials showed no decrease in mortality rate from EGDT compared with usual care, which did not mandate the more controversial components of the 2001 protocol (i.e., central venous oxygen saturation monitoring, blood transfusions, and inotropes).

Box 41.2 Updated Surviving Sepsis Campaign Bundle

- Complete within 3 hours of presentation
  - Measure lactate level
  - Obtain blood cultures prior to antibiotic administration
  - Administer antibiotics
  - Give 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L
- Complete within 6 hours of presentation
  - For hypotension unresponsive to fluid resuscitation, start vasopressors for MAP ≥ 65 mm Hg
  - Assess volume status and tissue perfusion if persistent hypotension (MAP < 65 mm Hg) or initial lactate ≥ 4 mmol/L
  - Repeat lactate if initial value was elevated

MAP, Mean arterial pressure.

The Surviving Sepsis Campaign (SSC) Executive Committee recently revised their guidelines because of the new evidence presented[19] (Box 41.2). Based on the current data, sepsis care should involve early aggressive intravascular fluid resuscitation targeting end points such as fluid responsiveness and lactate clearance (as opposed to central venous oxygen saturation monitoring or CVP measurements). Early antibiotic administration and source control are important components to sepsis management. Vasopressors can be used to support organ perfusion after intravascular volume repletion, and central lines should not be inserted in all patients unless indicated clinically.

Finally, goal-directed, liberal fluid administration during the acute phase of sepsis offers important benefits, but excess fluid is not beneficial when it is not physiologically needed during the established phase of sepsis. In the Fluid and Catheter Treatment Trial (FACTT) of patients with acute lung injury (mostly owing to pneumonia or sepsis), patients in the "conservative fluid" (i.e., minimal use of fluids) management group had improved lung function, improved central nervous system (CNS) function, and a decreased need for sedation, mechanical ventilation, and intensive care when compared to a liberal fluid group.[20] In addition, the patients in the conservative fluid management group did not have an increased incidence of complications, such as organ failure or shock. Perhaps the final lesson from all these studies is that management should be based on clinical examination findings and patient requirements as opposed to absolute numbers obtained by invasive monitors.

ACUTE RENAL FAILURE

Epidemiology

The incidence of acute kidney injury (AKI) in the ICU is highly variable and can be as high as 35%. Despite improvements in renal replacement technology, mortality rate caused by AKI in the ICU has remained at more than 50%.

Table 41.6 The RIFLE Criteria

RIFLE Category	GFR Criteria	UO Criteria	OR Hospital Mortality
Risk	Cr increased × 1.5 or GFR decreased >25%	UO <0.5 mL/kg/h × 6 h	2.2 (95% CI 2.17-2.3)
Injury	Cr increased × 2 or GFR decreased >50%	UO <0.5 mL/kg/h × 12 h	6.1 (95% CI 5.74-6.44)
Failure	Increased Cr × 3 or GFR decrease >75% or Cr > 4 mg/dL	UO <0.3 mL/kg/h × 24 h or Anuria × 12 h	8.6 (95% CI 8.07-9.15)
Loss	Complete loss of renal function For > 4 wk		
ESRD	End-stage disease		

Cr, Creatinine; *ESRD*, end-stage renal disease; *GFR*, glomerular filtration rate; *OR*, odds ratio; *UO*, urine output.
Data modified from Global KDI, Group OKAKIW. Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guideline for acute kidney injury. *Kidney Int.* 2012;(suppl 2):1-138.

Diagnosis

The definition of AKI has not been straightforward and multiple criteria are used in the literature. The Acute Dialysis Quality Initiative (ADQI) group, an alliance of experts consisting of nephrologists and intensivists, proposed the RIFLE criteria (Table 41.6), which stands for risk, injury, failure, and two outcome classes (loss and end-stage kidney disease).[21] For each increasing RIFLE class, there is a stepwise increase in mortality rate independent of a comorbid condition. Strategies to prevent even mild AKI may improve survival, and recovery of renal function in the ICU should be a specific therapeutic target.

Acute renal failure (ARF) is normally categorized by prerenal, renal, and postrenal causes (Box 41.3). The workup should include careful physical examination and assessment of intravascular volume status in order to differentiate hypovolemia leading to prerenal azotemia versus hypervolemia from oliguria. Laboratory evaluations should include serum and urine electrolytes, urinalysis, and examination of urinary sediment. Urine sodium concentration and fractional excretion of sodium can help identify prerenal azotemia. In patients who have received a diuretic, the fractional excretion of urea may be a more sensitive test than fractional excretion of sodium.

Treatment

Supportive care should be focused on maintenance of euvolemia, avoidance of nephrotoxic drugs, medication dose adjustments for creatinine clearance, and electrolyte and acid-base monitoring. Platelet dysfunction may occur as a result of uremia and require desmopressin (DDAVP) for support if bleeding is problematic. Pharmacologic approaches to improve renal function such as low-dose dopamine, diuretics, and *N*-acetylcysteine have not shown benefit. Dialysis is often required in patients with advanced renal failure to help with excessive intravascular volume and electrolyte disturbances.

Box 41.3 Causes of Acute Renal Failure

Prerenal
Hypovolemia
Low effective circulating volume (decompensated heart failure or liver disease)

Renal
Glomerulonephritis
Toxins (NSAIDs, cisplatin, aminoglycosides, contrast agent, myoglobin, hemoglobin)
Vasculitis (TTP/HUS)
AIN (PCN, cephalosporins, cimetidine, SLE, sarcoidosis)
Tubular disease (ATN, tumor lysis syndrome)

Postrenal
Obstructive nephropathy

AIN, Acute interstitial nephritis; *ATN*, acute tubular necrosis; *NSAIDs*, nonsteroidal antiinflammatory drugs; *PCN*, penicillin; *SLE*, systemic lupus erythematosus; *TTP/HUS*, thrombotic thrombocytopenic purpura/hemolytic uremic syndrome.

Dialysis

Dialysis in the ICU patient is often accomplished by continuous renal replacement therapy (CRRT). Although CRRT has several theoretical advantages over intermittent hemodialysis (IHD), randomized trials have not supported its superiority.[22] The difference in efficacy lies not in the type of dialysis (IHD vs. CRRT), but in the dialysis dose. Inadequate dialysis appears to be harmful, but intensive dose dialysis is also not beneficial in terms of mortality rate, renal function recovery, or ICU length of stay.[23,24] The important factor seems to be achieving the prescribed dose.

PAIN AND SEDATION

Pain and agitation are commonly underrecognized and undertreated in the ICU, yet there are important hemodynamic and psychological consequences associated with unrelieved pain and agitation, such as impaired wound healing, increased levels of catecholamines, and development of posttraumatic stress disorder (also see Chapter 40). Unfortunately, many patients in the ICU are unable to self-report pain and discomfort. Although vital signs may indicate the presence of pain and agitation, hypertension and tachycardia should not be used alone in the assessment.

Table 41.7 Commonly Used Sedatives and Analgesics

Drug	Elimination Half-Time	Peak Effect[a]	Suggested Dose
Morphine	2 to 4 h	30 min	1 to 4 mg bolus 1 to 10 mg/h
Fentanyl	2 to 5 h	4 min	25 to 100 μg bolus 25 to 200 μg/h
Hydromorphone	2 to 4 h	20 min	0.2 to 1 mg bolus 0.2 to 5 mg/h
Ketamine	2 to 3 h	30 to 60 s	1 to 5 ug/kg/min
Midazolam	3 to 5 h	2 to 5 min	1 to 2 mg bolus 0.5 to 10 mg/h
Lorazepam	10 to 20 h	2 to 20 min	1 to 2 mg bolus 0.5 to 10 mg/h
Propofol	20 to 30 h	90 s	25 to 100 μg/kg/min
Dexmedetomidine	2 h	1 to 2 min	0.2 to 0.7 μg/kg/h

[a]With intravenous administration.

Commonly used sedatives and analgesics are listed in Table 41.7 (also see Chapters 8 and 9). The choice of which drug to use should depend on the effect that is desired. Pain control should be treated with analgesics, whereas anxiolysis should be accomplished with sedatives. Specific concerns related to the use of these medications in the ICU will be addressed in the next sections.

Analgesia

Opioids are the first-line treatment for pain (also see Chapter 9). They can be administered by continuous infusion, as needed boluses, or patient-controlled methods if the patient is neurologically intact and not heavily sedated. Fentanyl is the most frequently used opioid in the ICU owing to its pharmacokinetics (e.g., relatively short duration of action) and lack of active metabolites. Methadone is a synthetic, long-acting opioid that has a unique place in the ICU. It is often administered to patients who have been receiving narcotic infusions for a prolonged time or who require large narcotic doses because of chronic pain. Because of its long half-life, methadone dose should be increased slowly to avoid oversedation. Methadone has been associated with QT-interval prolongation and torsades de pointes, so electrocardiogram (ECG) monitoring is essential for ICU patients.

Multimodal analgesia with nonopioid drugs may help limit the narcotic side effects and is encouraged in ICU patients. Adjuncts include acetaminophen, ketamine, antiepileptics (gabapentin and carbamazepine), α_2-adrenergic agonists (clonidine and dexmedetomidine), tramadol, antidepressants, and topical lidocaine. In addition, for postoperative pain, regional anesthesia techniques may also limit total narcotic dose (also see Chapter 40).

Sedation

Sedation is used in the ICU to provide anxiolysis, amnesia, and comfort and ensure the safety of life-sustaining interventions (e.g., inadvertent patient removal of central lines, ETTs, or drains). Sedatives can also assist with mechanical ventilator dyssynchrony, seizure control, intracranial pressure reduction, and alcohol withdrawal.

Benzodiazepines

Benzodiazepines are commonly administered for ICU sedation because they provide anxiolysis and anterograde amnesia. In addition, they are often used to prevent or treat seizures and alcohol withdrawal symptoms. Midazolam causes less ventilatory and cardiovascular depression when compared with propofol. However, benzodiazepines may contribute to the development of ICU delirium, especially in elderly patients.

Propofol

Propofol has pharmacologic properties such as rapid onset and relatively short duration of action, which are ideal for the mechanically ventilated ICU patient who requires frequent neurologic evaluation. It is also useful in treating seizures and decreasing intracranial pressure. Propofol has no analgesic effects, so an opioid may be necessary concurrently.

In addition, propofol decreases myocardial contractility and SVR, so it may not be the drug of choice in severely hypotensive patients. Because of its respiratory depressant effects, propofol should be used for sedation only in intubated patients or for procedural sedation in nonintubated patients with the presence of an anesthesia provider.

The propofol preparation contains lecithin and has a high fat content, so patients on prolonged infusions should be monitored for hypertriglyceridemia and the development of pancreatitis. For ICU patients on total parenteral nutrition, the propofol infusion needs to be accounted for when calculating caloric requirements.

Propofol infusion syndrome (PRIS) is a rare syndrome caused by mitochondrial dysfunction and characterized by metabolic acidosis, hyperkalemia, rhabdomyolysis, and fatty liver infiltration. Cardiac complications may

include nonspecific symptoms such as acute refractory bradycardia and right bundle branch block. It is more common in children, but predisposing factors include infusion rates of more than 5 mg/kg/h for more than 48 hours in patients with critical illness receiving vasopressors or glucocorticoids. Early recognition of the syndrome and discontinuation of the propofol infusion reduce morbidity and mortality rates, which can be as high as 80%.

α_2-Receptor Agonists

The sedative effect from dexmedetomidine resembles more of a physiologic sleep state than the other sedatives. In the ICU, a dexmedetomidine infusion of 0.2 to 1.2 µg/kg/h can be started without an initial bolus dose. Dexmedetomidine use in critically ill adults reduced the duration of mechanical ventilation and ICU length of stay compared with traditional sedatives such as propofol, midazolam, and lorazepam.[25]

N-Methyl-D-Aspartate Receptor Antagonist

A ketamine infusion (1 to 5 µg/kg/min) can be used in the ICU to limit opioid tolerance and provide analgesia without respiratory depression. Ketamine is also useful in small bolus doses (0.2 to 0.8 mg/kg IV) for patients who need to undergo brief, painful procedures (e.g., burn dressing changes). The sympathomimetic properties of ketamine are associated with better preservation of arterial blood pressure and heart rate, but ketamine is still a direct myocardial depressant and may lead to hypotension when given to patients in shock.

Sedation Interruption

Meta-analyses have not shown strong evidence for protocol-directed sedation and daily sedation interruption because of the heterogeneity between trials. However, lighter levels of sedation or daily sedation interruption (also called "sedation wake-up") are the expected standard instead of deep, uninterrupted sedation.[26] In single center studies, daily sedation wake-up with retitration led to shorter durations of mechanical ventilation and ICU lengths of stay when compared with weaning based on the discretion of the intensivist.[27,28] Rapid weaning of sedation did not increase complications such as unplanned tracheal extubation, myocardial ischemia, or delirium. Combining sedation wake-up with protocol-driven ventilator weaning reduced duration of mechanical ventilation, mortality rate, and ICU length of stay.[29] This practice has become the preferred method and the standard of care in most ICUs.

OTHER TOPICS IN CRITICAL CARE

Delirium

Delirium, characterized as an acute onset of waxing and waning mental status, occurs frequently in critically ill patients. Delirium can be divided into two subtypes, hyperactive and hypoactive. Hyperactive delirium is characterized by periods of agitation, restlessness, and emotional lability. This patient is often pulling out lines and catheters or hitting and biting. Hypoactive delirium is characterized by flat affect and apathy. Patients may seem calm and alert, but they suffer from the same cognitive changes as the hyperactive form. Both forms occur with equal frequency.

Delirium independently predicts ICU outcomes such as mortality rate, hospital length of stay, cost of care, and the development of post-ICU syndrome. All ICU patients should routinely be screened for delirium with tools such as the Confusion Assessment Method for the ICU (CAM-ICU) (Table 41.8).

The causes of delirium are numerous. Factors that can contribute to delirium in the ICU patient include

Table 41.8 Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) Delirium Assessment

CAM-ICU Worksheet	
Feature 1: Acute onset of mental status changes or a fluctuating course	
Feature 2: Inattention	Ask patient to squeeze your hand whenever he hears the letter "A." Read S...A...V...E...A...H...A...A...R...T.
	Points are given when patient squeezes on "A" and does not squeeze on other letters.
	This feature is positive if score is 8 or less
Feature 3: Disorganized thinking	Ask patient questions, 1 point for each correct answer.
	Will a stone float on water? Are there fish in the sea? Does one pound weigh more than two pounds? Can you use a hammer to pound a nail?
	Ask patient to hold up fingers on left hand and right hand: 1 point if able to successfully complete the entire command.
	This feature is positive if score is less than 4.
Feature 4: Altered level of consciousness	Considered positive if the RASS score is anything other than zero

Overall CAM-ICU is positive if Features 1 and 2 and either Feature 3 or 4 are positive.
RASS, Richmond Agitation-Sedation Scale.

preexisting cognitive impairment, advanced age, increasing severity of illness, multiorgan dysfunction, sepsis, immobilization, sleep deprivation, pain, mechanical ventilation, and the use of benzodiazepines. Nonpharmacologic prevention strategies, such as early mobilization, physical and occupational therapy visits, and reorientation help to reduce the incidence of delirium and improve other ICU outcomes. When these strategies are unsuccessful, antipsychotic medications, including haloperidol and atypical antipsychotics, may be administered, but their efficacy has yet to be adequately demonstrated in randomized controlled trials.[30]

Nutrition

The goal of nutrition in the ICU is to preserve lean body mass and avoid malnourishment, which can lead to increased mortality rate, prolonged hospital stay, poor wound healing, and increased risk for infection. However, there are no reliable laboratory markers to determine the patients at risk, because of fluctuating volume status and impaired protein synthesis associated with critical illness and multiorgan failure.

Estimates of daily caloric requirements can be calculated from various equations. The Harris Benedict equation estimates basal energy expenditure based on weight, height, age, and gender, but then adjustments must be made for the underlying disease processes such as infections, multisystem organ dysfunction, trauma, and burns. A quick estimate of whether the patient is receiving enough calories can be based on weight and level of stress or illness (Table 41.9). Sometimes, a simple nutritional plan can be started based on these estimates, and then further tests (e.g., nitrogen balance study) can be obtained to assess the adequacy of the protein-based calories.

Enteral nutrition is always preferred to parenteral nutrition in order to maintain gut integrity, but achieving goal rate or goal calories is not urgent, at least for the first week.[31] Vomiting and aspiration of gastric contents have long been a concern for critically ill patients fed via a feeding tube. In the past, feedings were often reduced or held for minimal gastric residual volume (GRV), leading patients to receive only a small portion of their estimated caloric requirement over time. Current literature does not support this practice, so significantly larger GRVs are now accepted (500 mL or more in some institutions).

Patients undergoing frequent surgeries (like burn débridements) may end up malnourished from frequent nutritional holds that start at midnight or 8 hours prior to surgery. With increased emphasis on continuing enteral nutrition, there has been a shift toward decreasing nil per os or nothing by mouth (NPO) times for critically ill patients having surgical procedures. One approach is to continue enteral feeding until just prior to transport to the operating room for patients receiving postpyloric or jejunal feeding.[32] At some institutions, this "short duration NPO" approach is also used for ICU patients with gastric tubes (oral, nasal, or percutaneous gastrostomy), with the added step of aspiration of the gastric tube with a syringe to empty the stomach prior to transport. Standard NPO times may still be necessary prior to procedures involving the airway (tracheostomies or laryngectomies). No definitive data exist to guide practice and ultimately the decision is based on a hospital's practice and the clinical discretion of the anesthesia provider.

Table 41.9 Quick Estimate of Caloric Needs

Level of Illness/Stress	Estimated Caloric Need
Maintenance or minimal	25-30 kcal/kg/day
Moderate	30-35 kcal/kg/day
Severe	35-40 kcal/kg/day

The nutritional intake composition should be 1.2-2 g/kg/day protein, 15% to 30% of calories should be from lipids, and the remainder of the calories should be from carbohydrates (30% to 70%).

Glucose Control

Based on a landmark 2001 study, intensive insulin therapy to achieve a blood glucose level between 80 and 110 mg/dL was thought to be essential for improving survival in the ICU.[33] However, more recent (2009, 2010) data have shown that intensive insulin therapy does not improve survival and actually increases the risks of hypoglycemia and mortality.[34,35] Currently, it appears that tight glycemic control, and even routine normalization of plasma glucose, may not be the right goal, and instead, moderate glucose levels (between 140 to 180 mg/dL) are more appropriate for the ICU patient. Using moderate glucose levels as a goal can minimize the risk of severe hypoglycemia (less than 40 mg/dL) and hyperglycemia (more than 200 mg/dL). The optimal glucose target is not known and will vary by patient, clinical scenario, and even rate of glucose change.

Prophylaxis

Venous Thromboembolism

Critically ill patients are at increased risk for venous thromboembolisms (VTEs), including deep vein thrombosis (DVT) and pulmonary embolism. Along with risk factors for the general population, independent risk factors specific to critically ill patients include mechanical ventilation, central venous catheterization, vasopressor administration, and platelet transfusion.

Randomized controlled trials reveal that chemoprophylaxis significantly reduces the occurrence of DVTs. Chemoprophylaxis may be achieved with unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH).[36] The American College of Chest Physicians recommends either UFH or LMWH in patients with moderate risk for VTE, whereas high-risk patients, such as trauma and orthopedic patients, should receive LMWH. In patients at increased risk for bleeding complications, mechanical thromboprophylaxis (e.g., graduated compression stockings, intermittent pneumatic compression devices) provides some level of protection against VTE, but it is less effective than chemoprophylaxis.

Gastrointestinal Prophylaxis

Gastrointestinal stress ulcers occur in critically ill patients owing to an increase in gastric acid production in conjunction with a functionally impaired mucosal barrier. Gastrointestinal bleeding occurs more frequently in patients who are mechanically ventilated for more than 48 hours and in those with a coagulopathy (Box 41.4). Patients in the ICU who are considered high risk for gastrointestinal hemorrhage should be started on prophylaxis. Either H_2 blockers or proton-pump inhibitors provide protection with the data somewhat favoring proton-pump inhibitors. Because of cost, an enteral route is preferred. The potential risks of developing hospital-associated pneumonia or *Clostridium difficile* infection because of an increased gastric pH should be weighed against the benefits in patients at risk for ICU-related gastrointestinal hemorrhage.

Hospital-Acquired Infections

The most common hospital-acquired infections (HAIs) in ICUs are urinary tract infections (31%), followed by pneumonia (27%), and primary bloodstream infections (19%). By reducing HAIs, hospitals can improve mortality rate and reduce cost. The Centers for Medicare and Medicaid Services no longer reimburse hospitals for additional costs associated with HAI.

Box 41.4 Indications for Gastrointestinal Prophylaxis

History of GI bleed within last year
Mechanical ventilation > 48 hours
Coagulopathy not from pharmacologic anticoagulation (platelet count < 50×10^9/L, INR > 1.5, or PTT > 2 × control)
Trauma
Spinal cord injury
Severe traumatic brain injury
Extensive thermal injury or burns
High-dose steroids in patients with severe sepsis or septic shock

GI, Gastrointestinal; *INR*, international normalized ratio; *PTT*, partial thromboplastin time.

Catheter-Associated Urinary Tract Infections

No single strategy prevents catheter-associated urinary tract infections. The only recommendations have been to use aseptic techniques for placement and to limit the duration of indwelling urinary catheters by assessing for daily need.

Ventilator-Associated Pneumonia

Positioning the head of the bed at 30 degrees is the most cost-effective intervention to prevent VAP. In patients anticipated to have a prolonged course of tracheal intubation with mechanical ventilation, the use of ETTs with subglottic suctioning appears effective for prevention. Excessive use of medications for stress ulcer prophylaxis increases gastric pH and increases the risk for VAP. Clinicians will need to balance the risks and benefits of using H_2-receptor antagonists or proton-pump inhibitors. The concept of preventing mechanical ventilation adverse events, including VAP, by use of a bundle (multiple single interventions implemented simultaneously) is common practice in many ICUs.[37]

Catheter-Related Bloodstream Infections

The prevention of catheter-related bloodstream infections (CRBSIs) is achievable through large-scale quality improvement projects that involve a bundle of evidence-based interventions. Recommendations include the use of ultrasound guidance for line placement, skin preparation with chlorhexidine, chlorhexidine sponge for site dressing, antimicrobial impregnated central lines, and maximal sterile barrier use during line placement. Broad implementation of these interventions can substantially reduce the risk and morbidity of these infections.[38]

ICU Staffing and Organization

Because of the increased complexity of care, ICUs have required more specialized staff, which can include physicians, nurses, nurse practitioners, physician assistants, respiratory therapists, physical therapists, pharmacists, nutritionists, and patient care assistants. The use of nonphysician providers, such as nurse practitioners and physician assistants under the supervision of attending critical care physicians, has become more prevalent with the institution of resident duty hour limitations in the United States. The presence of pharmacists reduces fatalities in patients with infections and sepsis, and the rate of adverse drug events. Respiratory therapist involvement improves compliance with weaning protocols and decreases duration of mechanical ventilation. The multidisciplinary team has been shown to improve mortality rate for critically ill patients.[39]

QUESTIONS OF THE DAY

1. A spontaneously breathing, mechanically ventilated patient is receiving pressure support ventilation. What determines the inspiratory flow rate and duration of each breath?
2. Which type of intensive care unit (ICU) patient is most likely to benefit from noninvasive positive-pressure ventilation (NPPV)? What are the most commonly encountered contraindications to NPPV?
3. What respiratory criteria predict successful weaning from mechanical ventilation? What nonrespiratory criteria can have an impact on the weaning process?
4. What mechanical ventilation strategy is most appropriate for a patient with acute respiratory distress syndrome (ARDS)?
5. What are the most common clinical conditions that can cause vasodilatory shock?
6. How can bedside ultrasonography be used to predict intravascular fluid responsiveness (improvement in blood pressure with intravenous fluid bolus) in a patient receiving positive-pressure ventilation?
7. In a patient who is mechanically ventilated, what is the impact of "sedation interruption" strategies on duration of ventilation and length of ICU stay?
8. What is the confusion assessment method for the intensive care unit (CAM-ICU) method of delirium assessment? What nonpharmacologic methods can help to prevent delirium in the ICU patient?
9. Which critically ill patients are most likely to develop gastrointestinal stress ulcers?
10. What are the most common hospital-acquired infections in the ICU?

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