Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Management of Patients with Acute Respiratory Distress Syndrome

JoAnne K. Phillips, RN, MSN, CCRN

Acute respiratory distress syndrome (ARDS) is a complex clinical syndrome characterized by noncardiogenic pulmonary edema and damage to the alveolar capillary membrane. This complex clinical syndrome was well described by Ashbaugh et al6 in 1967 in an article in which they described 12 patients with acute tachypnea, hypoxia, bilateral pulmonary infiltrates, and decreased pulmonary compliance from a variety of precipitating conditions, including trauma, sepsis, and aspiration.6 Over the past 30 years, research has more clearly defined the pathophysiology of ARDS, although the complexity of managing patients with this syndrome continues to present a challenge to the critical care team. Despite extensive research, the mortality rate associated with ARDS has only recently begun to decrease. Of the estimated 150,000 to 250,000 cases seen annually, the mortality rate continues to be approximately 50%. Deaths that occur in the first several days after the development of ARDS are most often associated with the precipitating event (e.g., sepsis or multiple trauma), whereas deaths that occur later are associated with respiratory failure from ARDS.10, 17, 21, 26, 30, 39, 48, 50 The complexity of this disease process necessitates a complete understanding of the pathophysiology to be able to understand the assessment priorities and to establish management strategies for patients with ARDS. This article addresses the pathophysiologic process associated with ARDS, describes physical assessment abnormalities, and assists the bedside clinician in establishing a clinical database for ARDS patients. Management strategies also exist for patients with complex syndrome.

Pathophysiology

Acute respiratory distress syndrome is a complex clinical syndrome characterized by noncardiogenic, high-permeability pulmonary edema, damage to the alveolar capillary membrane, and increased microvascular permeability. These physiologic abnormalities result in a clinical presentation of refractory hypoxemia, decreased lung compliance, and alteration in gas exchange. ARDS occurs as a clinical complication of critical illness from direct (pulmonary) or indirect (systemic) injury to the lungs.17, 23, 26, 28, 50 Examples of direct injury to the lung include20, 22, 45, 48:
- Inhalation injuries
- Gastric aspiration

From the Surgical Critical Care Unit, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania
Pulmonary contusion
Thoracic trauma
Pneumonia (viral, bacterial)
Emboli (fat, amniotic, thrombotic)
Near drowning
Examples of indirect injury include \textsuperscript{20, 22, 45, 48}
Sepsis
Shock
Multiple trauma
Disseminated intravascular coagulopathy (DIC)
Pancreatitis
Anaphylaxis
Multiple blood transfusions
Reperfusion injury
The complex disease process of "adult" respiratory distress syndrome was first described by Ashbaugh et al\textsuperscript{6} in 1967.\textsuperscript{10, 17, 28, 50} The investigators studied a group of 12 patients that presented with acute-onset tachypnea, refractory hypoxemia, loss of pulmonary compliance, and diffuse infiltrates on chest radiography. This clinical presentation resulted from a variety of precipitating events, including multiple trauma, sepsis, pulmonary infection, and gastric aspiration. The definition of this complex syndrome has continued to be controversial. To that end, in 1994 a European–American consensus conference was held, the results of which clearly defined ARDS. One key issue agreed on by the investigators was that the nomenclature for ARDS would be changed from "adult" to "acute" respiratory distress syndrome because the disease process is not limited to adults. The conference participants further defined ARDS as the acute onset of respiratory failure associated with an arterial oxygen pressure (Pa\textsubscript{O\textsubscript{2}})–fraction inspired oxygen (FIO\textsubscript{2}) ratio of < 200, bilateral fluffy infiltrates on chest radiograph, and a pulmonary capillary wedge pressure of 18 mm Hg or less.\textsuperscript{17, 23, 26, 28}

A broad spectrum of precipitating events is associated with the development of ARDS. Patients who experience sepsis (in particular, gram-negative sepsis), aspiration of gastric contents, pulmonary contusion, and multiple transfusions are at highest risk.\textsuperscript{46} Pepe et al\textsuperscript{37} reported an additive effect of risk factors, with ARDS developing in 25% of patients with one risk factor, in 42% of patients with two risk factors, and in 85% of patients with three risk factors.\textsuperscript{46, 47} (see earlier lists of direct and indirect injuries as risk factors).

Mediators

The systemic effects of ARDS occur as a result of the mediator cascade, inflammatory response, and subsequent fluid shifts associated with the pathophysiologic presentation. The mediator cascade is initiated in response to the patient's exposure to a stimulus, such as endotoxin. Endotoxin is released from the walls of gram-negative bacteria after injury, ischemia, or insult disrupts the cell wall, allowing its release (Fig. 1). Exposure to the inciting event stimulates the release of macrophages and monocytes. The release of these substances initiates the mediator cascade, which begins with the release of several cytokines, including tumor necrosis factor and interleukin, (IL) 1, IL-6, and IL-8. Both tumor necrosis factor and IL-1 promote adherence of activated neutrophils to the endothelial wall, in addition to amplifying the inflammatory process associated with ARDS.\textsuperscript{10, 50}

The initiation of the mediator cascade also stimulates the release of platelet-activating factor (PAF). The key functions of PAF are to activate platelets and neutrophils, which migrate to the lungs, where they adhere to the pulmonary endothelium, resulting in vasoconstriction and bronchoconstriction. The migration of platelets and neutrophils to the lungs also stimulates the release of bradykinin and histamine. Bradykinin and histamine increase capillary permeability, facilitating the shift of proteinaceous fluid from the pulmonary vasculature to the interstitium of the lung. PAF also has significant systemic effects, including increased blood pressure, increased pulmonary artery pressures, a negative inotropic effect, airway constriction, and potential activation of the coagulation system.\textsuperscript{49}

Neutrophils also play a key role in the development of ARDS by stimulating the release of proteases (proteolytic enzymes), free oxygen radicals, PAF, and metabolites of arachidonic acid. Proteases function to attract neutrophils to the pulmonary vasculature and, in doing so, amplify the inflammatory process associated with ARDS. They also damage the type 2 pneumocytes, where surfactant is normally produced, thus negating normal surfactant production. Proteases can also destroy normal lung tissue and the pulmonary vasculature.
The release of free oxygen radicals is also moderated by the neutrophils. Free oxygen radicals aggregate neutrophils to adhere to and injure the pulmonary vascular endothelium and interstitial tissue. The effects of the neutrophils on the pulmonary vascular endothelium lead to an increase in capillary permeability, facilitating the movement of proteinaceous fluid from the pulmonary vasculature into the interstitium.

Arachadonic acid is another mediator that plays a key role in the physiologic presentation of ARDS. Arachadonic acid is metabolized through two different pathways: (1) the cyclo-oxygenase pathway and (2) the lipo-oxygenase pathway. The cyclo-oxygenase pathway produces prostacyclin and thromboxane A2. Prostacyclin produces a vasodilatory effect that normally balances with the vasoconstricting effects of thromboxane A2. Thromboxane A2 produces pulmonary vasoconstriction and bronchoconstriction and also plays a role in the aggregation of platelets. The metabolism of arachadonic acid through the lipo-oxygenase pathway produces leukotrienes and lipoxines. Further aggregation of neutrophils, which produce bronchoconstriction and pulmonary vasoconstriction, occurs.

Products of arachadonic acid metabolism (i.e., platelets, fibrin thrombi, and leukocytes) may account for the pulmonary hypertension often seen in patients with ARDS.

**Fluid Shifts**

Another pathophysiologic process associated with the development of ARDS is the process by which fluid transudates from the pulmonary vasculature into the lung interstitium and into the alveoli (Fig. 2). PAF, a key mediator in the development of ARDS, activates platelets and neutrophils to release bradykinin and histamine, which result in an increase in capillary permeability. Within 24 hours of injury, the change in permeability allows the transudation of proteinaceous fluid from the pulmonary vasculature into the pulmonary interstitium (see Fig. 2). The fluid contains proteolytic enzymes, free oxygen radicals, metabolites of arachidonic acid (thromboxane A2), platelets, serotonin, activated neutrophils, and PAF. Normally, this fluid is drained by the lymphatic system, with no further clinical consequences. But in patients with ARDS, the lymphatic system quickly becomes overwhelmed and is unable to drain the fluid. The
fluid overload in the pulmonary interstitium results in decreased functional residual capacity; narrowing of small airways; and decreased compliance, culminating in an increased work of breathing. The fluid then transudates into the alveoli, with resulting alveolar edema. The type 1 alveolar cells swell and are not able to participate in gas exchange. Type 2 cells then proliferate but unfortunately become dysfunctional, negating the normal production of surfactant. A thorough understanding of the physiologic effects of the mediator cascade and fluid shifts is vital to integrate assessment data and management strategies for this complex patient population.

**Integration of Assessment Data**

Assessment of patients at risk for ARDS begins with examination of the direct and indirect risk factors (see earlier lists). Increasing risk for ARDS is related to the number of risk factors implicated. The progression of the three interrelated phases of ARDS correlates with physical assessment and clinical data.

The initial phase is referred to as the *acute exudative phase*, which can begin as early as 24 hours after the initial insult and last up to 7 days. It is characterized by parenchymal surface hemorrhage and capillary congestion. Proteinaceous fluid that transudates from the vasculature into the interstitium is normally drained by the lymphatic system. In the initial phase of ARDS, the lymphatic system is overwhelmed and unable to drain the proteinaceous fluid, resulting in interstitial edema. Without appropriate drainage, the fluid continues to transudate into the alveoli, resulting in alveolar edema, destruction of the type 1 alveolar cells, and early formation of a hyaline membrane over the alveoli. The associated clinical presentation is delineated in Table 1.

In the second phase, the proliferative phase, patients present with acute respiratory failure. Further destruction of the type 1 alveolar cells occurs, and they are replaced by type 2 alveolar cells. Surfactant is normally produced by the type 2 cells; however, the type 2 cells become dysfunctional, with a loss of surfactant production. The lack of surfactant leads to an increase in alveolar dead space, with
resulting venous admixing and an increased shunt fraction, the clinical results of which are refractory hypoxemia, increased peak inspiratory pressures, and decreased compliance. The third and final phase is known as the fibrotic phase. In this phase, interstitial fibrosis develops. Increased dead space ventilation is evidenced by increasing arterial carbon dioxide pressure.39, 49, 50

Management Strategies
The complexity of the disease process of ARDS lends itself to complex management priorities. As previously noted, outcomes from ARDS have not improved significantly over the past 20 years. Thus, management strategies for this complex disease process are clearly multifaceted. The goals for the management of patients with ARDS are:

1. **Preventive**: Rapid identification of patients at risk for ARDS based on the direct and indirect precipitating factors. Some causative factors cannot be prevented (e.g., massive transfusion after major trauma), whereas others can be (e.g., gastric aspiration).

2. **Cardiorespiratory support and resuscitation**: Aggressive support and

### Table 1 Physiology and Associated Physical Examination

| Phase          | Physiology                                      | Physical Examination                        |
|----------------|-------------------------------------------------|--------------------------------------------|
| Exudative phase| Parenchymal surface hemorrhage                  | Restless, apprehensive, tachypneic          |
|                | Interstitial or alveolar edema                   | Respiratory alkalosis                       |
|                | Compression of terminal bronchioles             | Pao$_2$: normal                            |
|                | Destruction of type 1 alveolar cells             | CXR: normal                                |
|                |                                                 | Chest examination: moderate use of accessory muscles, lungs clear |
|                |                                                 | Pulmonary artery pressures: elevated       |
|                |                                                 | Pulmonary capillary wedge pressure: normal or low |
| Proliferative phase | Destruction of type 2 alveolar cells              | Pulmonary artery pressures: elevated       |
|                | Gas exchange compromised                         | Increased workload on right ventricle       |
|                | Increased peak inspiratory pressure              | Increase use of accessory muscles           |
|                | Decreased compliance (static and dynamic)       | Fine crackles or rales                      |
|                | Refractory hypoxemia                             | Increasing agitation related to hypoxia     |
|                | • Intra-alveolar atelectasis                     | CXR: interstitial or alveolar infiltrates; elevated diaphragm |
|                | • Increased shunt fraction                       | Hyperventilation; hypercarbica              |
|                | • Decreased diffusion                            | Decreased SVO$_2$                           |
|                | • Decreased functional residual capacity         | Widening alveolar-arterial gradient         |
|                |                                                 | Increased work of breathing                 |
|                |                                                 | Worsening hypercarbica and hypoxemia       |
|                |                                                 | Lactic acidosis (related to aerobic metabolism) |
|                |                                                 | Alteration in perfusion                     |
|                | • Increased heart rate                           | • Increased heart rate                      |
|                | • Decreased blood pressure                       | • Decreased blood pressure                  |
|                | • Change in skin temperature and color           | • Change in skin temperature and color      |
|                | • Decreased capillary filling                    | • Decreased capillary filling               |
|                | End-organ dysfunction                            | End-organ dysfunction                       |
|                | • Brain: change in mentation, agitation,         | • Brain: change in mentation, agitation,    |
|                | hallucinations                                  | hallucinations                             |
|                | • Heart: decreased cardiac output $\rightarrow$ angina, | • Heart: decreased cardiac output $\rightarrow$ angina, |
|                | • Renal: decreased urinary or GFR                | CHF, papillary muscle dysfunction, arrhythmias, MI |
|                | • Skin: mottled, ischemic                        | • Renal: decreased urinary or GFR           |
|                | • Liver: elevated SGOT, bilirubin, alkaline      | • Skin: mottled, ischemic                   |
|                | phosphatase, PT/PTI; decreased albumin           | • Liver: elevated SGOT, bilirubin, alkaline |

Pao$_2$ = arterial oxygen pressure; CXR = chest radiograph; CHF = congestive heart failure; MI = myocardial infarction; GFR = glomerular filtration rate; PT = prothrombin time; PTT = partial thromboplastin time.

Data from references 19, 25, 32, 38, 45, 48, and 49.
monitoring of fluid administration and oxygen delivery. Correct physiologic abnormalities that present a threat to end-organ function.23

3. **Prevent complications:** Monitor end-organ function; prevent other complications, including barotrauma, ventilator-associated nosocomial pneumonia, line sepsis, sinusitis, gastrointestinal bleeding, and oxygen toxicity.30

---

**Hemodynamics**

The use of a pulmonary artery catheter and integration of the pathophysiology of ARDS provides clinicians with information that enables the team to formulate a plan for patient management. A pulmonary artery catheter is vital in monitoring indices of preload (i.e., central venous pressure and pulmonary capillary wedge pressure [PCWP]) and afterload (i.e., systemic vascular resistance and pulmonary vascular resistance) and contractility (i.e., left and right ventricular stroke work indices).

Although no hemodynamic profile is diagnostic for ARDS, a normal PCWP and a normal or slightly elevated cardiac output are characteristic of ARDS.22 The physiologic effects of the mediator cascade in combination with the physical effects of mechanical ventilation are demonstrated in the hemodynamic profile obtained from the pulmonary artery catheter:

1. Right ventricular preload is decreased as a function of decreased venous return to the right heart.
2. Right ventricular afterload is increased as a function of increased resistance in the pulmonary vasculature (i.e., hypoxic vasoconstriction, mediator-induced pulmonary vasconstriction, and increased pulmonary vascular resistance). Decreased right ventricular output results.
3. Left ventricular preload is decreased from the effects of increasing levels of positive end-expiratory pressure (PEEP). Left ventricular stroke volume may also be decreased from the effects of PEEP.49
4. Myocardial contractility may be negatively affected by PAF, acidosis, hypoxia, or myocardial depressant factor associated with sepsis.25

Hemodynamic data interpretation requires a comprehensive patient analysis, including the evaluation of the level of PEEP, patient position, and therapeutic interventions that may affect the hemodynamic profile, such as fluid administration or inotropic support. When the assessment is complete, therapeutic goals are set for the patient. Goals for fluid management are to optimize cardiac output and blood flow while avoiding an elevated PCWP.23,30 Elevations in PCWP can lead to further transudation of fluid from the pulmonary capillaries to the interstitium, which can result in increased pressure on smaller airways, decreased functional residual capacity, and increased work of breathing. The fluid can further transudate into the alveoli, causing alveolar edema, dysfunction of type 1 and type 2 pneumocytes, and decreased surfactant production (Fig. 2).

Optimization of cardiac output and oxygen delivery can be achieved through two mechanisms. The assessment of optimal cardiac output and PCWP can be accomplished with the calculation of the Starling curve. This calculation enables bedside clinicians to identify what PCWP will optimize the cardiac output. Fluid therapy, which can include crystalloid or colloid administration, can be adjusted to maintain the optimal cardiac output. When the patient has been adequately volume resuscitated and the optimal PCWP has been identified, the conventional theory on managing patients with ARDS is to keep them "dry."46 Judicious administration of fluids must provide intravascular support but also maintain optimal PCWP as determined by the calculation using the Starling curve. Humphrey et al24 and Schuller et al42 demonstrated that a decreased incidence of pulmonary edema and negative fluid balance in patients with ARDS contributed to improved survival and decreased intensive care unit (ICU) length of stay (LOS).

The second mechanism by which cardiac output and subsequent oxygen delivery can be optimized is through the use of inotropic agents, including dopamine (Intropin), dobutamine (Dobutrex), and amrinone (Inocor).50 Assessment of the effectiveness of increasing cardiac output on oxygen delivery can be accomplished through the calculation of the FICK equation, which uses cardiac output (Q), hemoglobin (Hgb), and the oxyhemoglobin-
bin saturations of arterial (SaO₂) and mixed venous blood (SvO₂):

\[ \text{Vo}_2 = 13.4 \times Q \times \text{Hgb} \times (\text{SaO}_2 - \text{SvO}_2) \]

In addition, determining the adequacy of tissue perfusion includes assessing the level of consciousness, cardiac rhythm, increased respiratory rate, peripheral and central cyanosis, cool skin, and decreased urine output. Refer to table 1 for assessment of end-organ dysfunction.

Therapies that normally improve cardiac performance and oxygen delivery, such as afterload reduction, are ineffective in patients with ARDS. Therefore, in addition to optimizing oxygen delivery, controlling consumption is important. One method by which oxygen consumption is controlled is through the use of sedatives, analgesics, and paralytic agents. The use of these agents helps to manage ventilator asynchrony, fear, anxiety, and pain. Nursing interventions that have been known to increase oxygen consumption, including suctioning, bed baths, weights, and dressing changes, must be assessed, and the absolute need for each of these interventions in the face of critical oxygen debt must be determined. Another physiologic problem that results in increased oxygen consumption is an elevated temperature, which increases oxygen consumption 10% per 1°C. The nurse at the bedside contributes significantly to assessing and managing patients’ oxygen consumption.

**Ventilator Management**

Mechanical ventilation is an integral part of managing patients with ARDS. A discussion of the wide range of ventilators and ventilator settings used to manage patients with ARDS is beyond the scope of this article. Therefore, this section focuses on the use of PEEP and pressure control with or without inverse ratio ventilation, both of which are considered standard for patients with ARDS. Interestingly, the use of both of these therapies to improve outcomes is not supported by research.

Traditional ventilator management has been the use of flow-controlled, volume-cycled ventilation, with 10 to 15 mL/kg of tidal volume and an inspiratory—expiratory ratio of 1:2 to 1:5; however, delivering 10 to 15 mL/kg tidal volume to a severely injured lung in the face of a markedly reduced lung volume (decreased by one third to one half) results in overventilated and overdistended alveoli. Overall, the goals for mechanical ventilation are to limit \( \text{FIO}_2 \) and maintain mean airway pressure while preventing complications such as hemodynamic compromise, fluid retention, and barotrauma. New strategies for mechanical ventilation are designed to use pressure-targeted ventilation, limiting tidal volumes and plateau pressure, allowing an elevated \( \text{PCO}_2 \) if necessary; adjust the level of PEEP to increase \( \text{PaO}_2/\text{FIO}_2 \); and to keep PEEP above the lower inflection point of the volume pressure curve.

**Positive End-Expiratory Pressure**

The work by Ashbaugh et al in 1967 suggested the use of PEEP to increase the \( \text{PaO}_2 \) in patients with ARDS. Since that time, PEEP has been used as an adjunct to ventilator support. The optimal level of PEEP has yet to be established. Marinelli and Ingbar described the strategies and goals of differing levels of PEEP:

1. **Best PEEP:** Highest static lung compliance
2. **Optimal PEEP:** Lowest shunt fraction
3. **Preferred PEEP:** Highest oxygen delivery (Do₂)
4. **Least PEEP:** Least PEEP necessary to reduce \( \text{FIO}_2 \) to below toxic range

In managing patients on PEEP, the level of PEEP should start at physiologic levels (3–5 cm water) and be systematically increased until positive effects have been achieved. With each change in the level of PEEP, a hemodynamic profile should be obtained after 15 to 30 minutes on the increased level of PEEP. This assessment includes cardiac output, arterial blood gas, blood pressure, \( \text{SvO}_2 \), pulmonary capillary wedge pressure, and compliance. Monitoring of pulmonary compliance is one way to determine the optimal effects of increasing PEEP. When compliance is no longer improving, further increases in PEEP probably will not produce increases in oxygenation. Bedside clinicians can use the following information to understand the expected hemodynamic consequences from increasing levels of PEEP.
Positive Effects of PEEP
Recruits previously closed alveoli
Stabilizes and expands fluid-filled alveoli
Decreases intrapulmonary shunt
Improves compliance
Enhances lung volume
Increases functional residual capacity
May offset shear forces associated with repeated collapse and reopening of recruitable alveoli

Negative Effects of PEEP
Increases intrathoracic pressure, resulting in decreased cardiac output and oxygen delivery
High levels of PEEP:
- Overdistended airways
- Obliteration of adjacent alveolar capillaries
- Increased alveolar dead space
- Worsening oxygenation
- Increased pulmonary vascular resistance leading to pulmonary hypertension
- Decreased left ventricular compliance
- Decreased venous return
- Decreased right ventricular preload; increased right ventricular afterload
- Decreased left ventricular preload

The expectation is that the patient will exhibit a significant increase in Pao2 with less than a 25% decrease in cardiac output. Unfortunately, no randomized studies delineate which level of PEEP would maximize patient outcome.

Pressure-Controlled Inverse Ratio Ventilation
The trend in ventilator management of patients with ARDS is away from volume-cycled ventilation to pressure-limited ventilation. Volume-cycled ventilation delivers gas in a constant square flow pattern, resulting in turbulent flow during the respiratory cycle. The gas takes the path of least resistance and fills alveoli that are open rather than expanding to noncompliant lung units, resulting in uneven gas distribution. The resulting barotrauma can lead to complications, such as pneumothorax. Pressure-cycled flow patterns deliver a decelerating gas flow, resulting in improved gas distribution and alveolar filling, leading to decreased minute ventilation requirements.

Pressure-controlled ventilation delivers a fixed or preset pressure to the airway for a given time or percentage of the respiratory cycle. The delivered tidal volume is variable and is dependent on the lung compliance and airway resistance. A constant inspiratory pressure is present, with a lengthened inspiratory time, changing the inspiratory-expiratory ratio from 1:2 or 1:1, to as high as 4:1. The benefits of pressure-controlled, inverse-ratio ventilation (PCIRV) include improved oxygenation; decreased peak inspiratory pressures, decreased minute ventilation, and decreased need for PEEP. The overall goal of PCIRV is to maintain mean airway pressure, recruit nonaerated alveoli, and facilitate gas exchange. Mean airway pressure can be raised by increasing minute ventilation, increasing end-expiratory alveolar pressure, or extending inspiratory time. An approximate linear relationship exists between mean airway pressure and arterial oxygenation, thus, increases in mean airway pressure result in increases in arterial oxygenation.

The ongoing assessment of patients on PCIRV differs from standard ventilation. Changes in airway resistance and pulmonary compliance do not result in increased peak inspiratory pressures but rather in decreased tidal volume because tidal volume is a function of airway resistance and compliance. Bedside assessment of tidal volume, oxygenation, end-tidal carbon dioxide, and pulse oximetry are key in assessing the effectiveness of ventilation. The ventilator also provides nurses at the bedside with information on compliance and shunt measurements, which assists with assessing the adequacy of the ventilator settings. Some differences from standard ventilator assessments when using PCIRV are:

- **Tidal volume:** Approximately 5 to 8 mL/kg
- **Pressure level:** Adjusted to obtain desired tidal volume
- **Inspiratory-expiratory ratio:** Change from traditional 1:2 to 1:1 to 1:4
- **Total PEEP:** Set PEEP plus auto-PEEP, which results from a combination of inspiratory time, rate, and pressure level. Auto-PEEP results in incomplete exhalation.
- **Compliance:** Ongoing monitoring of compliance to assess the effectiveness of increasing levels of PEEP
- **Overall assessment:** Hemodynamic, oxygen consumption
Despite advances in critical care, the need for further research into optimal ventilator settings continues. The research has not been able to demonstrate improved outcomes from either PEEP or PCIRV.

**Patient Positioning**

Nurses play a pivotal role in the management of patients with ARDS, especially the positioning of critically ill ARDS patients. In addition to the risk for multiple organ dysfunction syndrome, the pulmonary system presents several immobility-related potential complications for acutely ill ARDS patients. These complications include, but are not limited to, atelectasis, decreased tidal volume, impaired mucociliary escalator function, pneumonia, and pulmonary embolism. The role of the nurse at the bedside is to prevent as many complications as possible, keeping in mind the goals for managing patients with ARDS: to improve gas exchange, decrease shunt fraction, and provide cardiovascular support.

Two positioning strategies affect both sets of goals: (1) continuous lateral rotation therapy (CLRT) and (2) prone positioning.

**Continuous Lateral Rotation Therapy**

Continuous lateral rotation therapy may be provided on a lateral rotation table, with the patient turning through an arc of 124°, or on a lateral rotation cushion bed, rotating the patient to either 60° or 90° in both directions. The benefits of CLRT include improved mucociliary clearance, opening of alveoli in dependent lung zones, improvement in ventilation-perfusion mismatch, and the possible prevention of atelectasis. Basham et al presented a meta-analysis of six studies evaluating the effectiveness of CLRT. Their analysis showed a significant decrease in nosocomial pneumonia, atelectasis, the number of hours intubated, and ICU LOS. No significant effect was found in the development of ARDS, pressure ulcers, pulmonary embolism, mortality, or hospital LOS. Even though these studies showed no direct effect on the development of ARDS, the decrease in the incidence of pneumonia and ICU LOS could play a key role in decreasing risk factors for ARDS, which include pneumonia and sepsis. A cost analysis by Summer et al demonstrated a potential 35% decrease in ICU costs with the associated decreased use of mechanical ventilators and ICU LOS.

Indications for the placement and removal criteria for lateral rotation therapy beds include:
- \( \text{PaO}_2-\text{FiO}_2 \) ratio of less than 300 (demonstrating acute lung injury)
- Risk for ARDS (e.g., septic shock, aspiration, or multiple trauma)
- Intolerance to activity (e.g., sustained desaturation or change in heart rate or blood pressure)
- Required frequent bronchoscopy for secretion removal
- Open abdomen or chest
- Nitric oxide therapy; extracorporeal membrane oxygenation

**Prone Positioning**

Despite this information, more research is necessary. The cost of using continuous lateral rotation therapy (approximately $150/d) on every patient who may benefit requires definitive, clear cost-benefit analysis. The research must focus on which patients would benefit, when to initiate therapy, when to terminate therapy, and how to gain the greatest therapeutic advantage from CLRT.

Another positioning adjunct is the use of prone positioning. To understand why prone positioning is beneficial, one must refer back to the pathophysiology of ARDS. Patients with ARDS experience a significant ventilation-perfusion mismatch. Ventilation is a function of compliance, airway resistance, and gravity. When a patient is lying supine, gravity results in areas of consolidation in the dorsal (dependent) regions of the lung. Because air takes the path of least resistance, ventilation is deferred from the dependent (better-perfused) regions of the lungs to the anterior lungs. Perfusion, on the other hand, is best in the posterior lung regions, also because of gravity. Thus, keeping patients in a supine position may worsen the ventilation-perfusion mismatch, increasing the shunt fraction.

Turning patients prone shifts these densities from the posterior regions to the anterior regions. This improves ventilation in dependent lung zones, thus decreasing shunt fraction. Several theories as to why this is effec-
tive, although none have been completely researched in the literature, include:

**Blood flow redistribution:** Blood flow may be redistributed to recruited alveolar space with an increase in lung units with normal ventilation and perfusion.

**Ventilation redistribution:** Improved shunt fraction and increased blood flow to areas with normal ventilation and perfusion.

**Hydrostatic pressure changes:** Hydrostatic pressure is higher in dependent lung regions; therefore, "lung edema" is greater. Proning may cause progressive decrease in edema.

**Functional residual capacity:** Increased functional residual capacity is theorized but not proven.²⁹

The mechanics of turning critically ill patients prone present a challenge to the critical care team. Two techniques are currently used to turn critically ill patients prone. One is the use of a turning and support frame that facilitates the positioning patients in the prone position on a regular hospital bed. This device, the Vollman Prone Positioner (Hill-Rom, Batesville, IN), enables patients to be turned and positioned prone by three staff members.³¹ Using the manual method, at least five team members are necessary. Regardless of which method is used, a full assessment must be completed before such an intervention is undertaken. The assessment should include hemodynamic and oxygen consumption status to ensure that the patient is optimally supported and monitored. Knowing the baseline assessment enables the team to assess the success of the intervention. Further patient assessment includes the security of the airway (whether endotracheal, nasotracheal, or tracheostomy tube); the position of the ventilator tubing should be noted to ensure that it safely turns with the patient. The team member at the head of the bed is responsible for ensuring that the airway is secure and the ventilator tubing is properly placed during the turning process. Lines and drainage tubes should be directed toward the patient’s head (if above the waist), or toward the feet (if below the waist). The exception would be chest tubes, which are directed toward the feet. For the teams that are not using a metal frame for proning, the following is a suggested technique to help safely prone and position the patient:

1. **Assemble the troops:** The decision to turn a patient prone is collaborative, involving physicians, nurses, and respiratory therapists. The actual technique in turning the patient requires coordination between all team members. If the team is not experienced at proning, it would be advisable to have a resource available to reintubate the patient in the case of accidental extubation. The patient’s eyes should be lubricated and covered before turning.

2. **Equipment availability:** A lateral rotation bed is recommended; a new sheet should be placed on top of the patient before turning. New patient gown; cardiac monitoring leads; two bolsters to place under patient when he or she is prone; foam pillow to support the head and face; and extension tubings if necessary, should be used.

3. **Patient preparation:** The patient gown is removed. Position of invasive lines, airway, and ventilator tubing is ensured. Two team members are on each side of the bed, with the team leader at the head of the bed, facilitating the security of the airway.

4. **Initiate turn:** The patient is slid to the side of the bed, away from the ventilator (patient is always turned toward the ventilator). The arm that is now at the center of the bed should be tucked underneath the patient, using extra caution if an arterial line is present in that extremity. The outside leg is crossed over the inside leg at the ankle to facilitate turning.

5. **The patient is tilted** up on his or her side at a 45° angle, and the position of all invasive lines, drainage tubings, and the airway is reassessed.

6. **Positioning:** The patient is then placed onto his or her abdomen, placing the bolsters in one of two positions: (1) they can be safely placed from iliac crest to iliac crest and clavicle to clavicle or (2) clavicle to iliac crest on both sides. The goal of placing the bolsters is to suspend the abdomen to facilitate respiratory excursion.

7. **Head position:** The patient’s head is positioned toward the ventilator. The patency of the airway is checked by suctioning. The face is placed on the foam...
pillow, ensuring no pressure on the eyes to prevent injury.

8. **Recheck all invasive lines and tubings:** The arms are placed in a slightly flexed position next to the patient's head. Hourly reassessments of pressure on the patient's face and eyes are vital.

9. **Odds and ends:** Monitoring leads are replaced on the patient's back for easy access. Patient gown is replaced. Feet and ankles are propped to avoid pressure on the instep.

When the patient is placed in the prone position, evaluating the patient response can be based on the following criteria:

- $\text{SpO}_2$ increases within 5 minutes
- $\text{SvO}_2$, heart rate, and blood pressure return to baseline within 5 minutes
- Respiratory rate (RR) less than 30 and absence of accessory muscle use
- Arterial blood gases: Increased $\text{Pao}_2$ and oxygen saturation within minutes of position change, with no change in arterial carbon dioxide pressure

While in the prone position, the patient must be monitored for complications, including increased eye pressure, corneal abrasion; ulnar and perineal nerve damage; and skin breakdown on the penis, breast, or face. The literature is unclear about time intervals for position changes. Although some literature sites patients prone for 2 hours, other literature supports 20 hours or longer in the prone position. Prone positioning is an exciting adjunct in the care of critically ill patients with ARDS.

**Alternative Interventions**

As mentioned earlier, the management of patients with ARDS is multifaceted. The strategies mentioned up to this point have focused on hemodynamics, ventilator management, and patient positioning. Because the hallmark of ARDS is refractory hypoxemia, it is not unusual for patients to be unresponsive to the previously mentioned interventions, requiring the clinicians to take a more aggressive step in helping patients to survive this crisis. Two interventions used in managing patients with ARDS are extracorporeal membrane oxygenation and inhaled nitric oxide. Although these therapies are not available at all centers, all critical care nurses should be familiar with what interventions are available to ARDS patients in crisis.

**Extracorporeal Membrane Oxygenation**

One of the alternative interventions for patients with ARDS is extracorporeal membrane oxygenation (ECMO), a form of cardiopulmonary bypass in which blood is removed from the patient and travels through large membrane lung, at which time carbon dioxide is removed and oxygen is added. The blood is then rewarmed and reinfused into the patient. This process relieves the lungs of gas exchange requirements, facilitating lung rest.

The initial research in using ECMO for ARDS was carried out under a National Institutes of Health grant in 1979 by Zapol et al. The patients selected for this study had a predicted 90% mortality rate. No significant difference was found in the outcomes of patients managed with ECMO (9.8% survival rate) and those managed with conventional therapies (8.3% survival rate). In 1986, Gattinoni et al reported a survival rate of 49% in adults managed with extracorporeal carbon dioxide removal (ECCO2R), which is a technique similar to ECMO, using veno-venous bypass for carbon dioxide removal combined with low-frequency, positive-pressure ventilation. Although ECMO has been the standard of care for neonates with respiratory failure since...
1986, it is still used as rescue therapy in adults. More recent studies are demonstrating an improved outcome through better patient selection, shorter previous ventilator days, predominance of the veno-venous approach, and the use of low-pressure ventilation.13

Patient selection is a key factor in the success of ECMO. In general, patients being considered for extracorporeal support are patients who have failed traditional ventilatory support efforts and are demonstrating worsening hypoxemia. When assessing the appropriateness for a patient to be placed on extracorporeal support, the clinician must enlist a detailed history of the present problem, focusing on the severity of the respiratory failure, how long the patient has been ventilated, and the reversibility of the respiratory failure. Selection criteria and contraindications include5,13,14:

**Selection Criteria**
- Age of less than 60 years
- Reversible pulmonary disease
- Normal clotting
- Intact neurologic status
- Ventilated less than 5 days (10 day maximum)
- No major immunosuppression
- Absence of terminal disease
- Static lung compliance of less than 0.5 mL/cm H2O/kg
- Transpulmonary shunt of more than 30% on 60% FiO2

**Contraindications**
- FiO2 100%; more than 10 cm PEEP
- Contraindications to heparinization
- Multiple organ dysfunction syndrome (MODS)
- Poor quality of life
- Necrotizing pneumonia

The ECMO circuits provide either veno-arterial support or veno-venous support. The veno-arterial circuit, which provides cardiac and respiratory support, drains from the right internal jugular, right common iliac, or femoral vein and returns through the common carotid artery. The patient runs the risk for embolism into the arterial circuit, as well as the potential problems with ligating the carotid artery. The veno-venous circuit, which provides only respiratory support, drains from the right internal jugular vein or common femoral vein and returns through the right internal jugular or femoral vein.14

Supporting patients on ECMO is a resource-intensive process from the perspective of personnel, supplies, and blood products. Each patient is cared for by a specially trained registered nurse who focuses on the care of the patient. The patient is also cared for by an ECMO specialist, who is a specially trained registered nurse; respiratory therapist; or perfusionist who focuses on the management of the pump.

The care of patients on ECMO requires meticulous observation and acute assessment skills by the ECMO specialist. The care of the patient focuses on prevention of the following complications:

**Neurologic:** Patients are typically paralyzed and sedated; hourly neurologic checks are necessary to monitor for intracranial hemorrhage.

**Anticoagulation:** Activated clotting times are monitored every hour, with the goal of keeping the activated clotting time 180 to 200 seconds. The patient is heparinized during the initial cannulation procedure and is kept fully heparinized during the course of treatment. Bleeding is a frequent complication.

**Blood products:** Frequent blood product replacement is needed for bulk loss, consumption (platelet aggregation in the oxygenator), and sequestration of platelets in the liver and spleen. The nurse is responsible for monitoring the patient for bleeding or oozing at insertion sites, as well as serial blood samples to assess hemoglobin and hematocrit levels. Patient goals: Hematocrit, 40% to 45%; platelet count, more than 100,000 mm³ (or higher if necessary to prevent bleeding).

**Fluid management:** Many critically ill patients are volume overloaded at the initiation of extracorporeal support. Early management priorities include diuresis, either by administration of diuretic agents or the use of a dialyzer or hemofilter placed within the ECMO circuit. Fluid is administered at approximately 80% of maintenance.5

**Respiratory management:** ECMO is designed to provide "lung rest"; thus, ventilator settings provide minimal support, allowing most oxygenation and ventilation to take place within the ECMO cir-
Vigorous pulmonary toilet is still essential; thus, the incorporation of continuous lateral rotation therapy and prone positioning is key.

Although more detailed aspects are involved in caring for patients on ECMO, these are the outstanding priorities. Some of the overall benefits of ECMO include the reduction of pulmonary artery pressures and improved oxygenation and carbon dioxide removal, as well as decreased barotrauma by reduced high tidal volumes and high levels of inspired oxygen. The disadvantages include high cost and invasiveness. An institutional commitment must be made to provide this therapy because it requires the constant readiness of the ECMO team, which includes the surgeon, nurses, ECMO specialists, and respiratory therapist. The readiness of the team to provide 24-hour care comes with a price because ECMO adds conservatively $3000 per day to patients' hospital bills. Although this therapy may provide an improved outcome for some patients, the selection of which patients are appropriate is vital for the success of the program.

**Nitric Oxide**

One of several experimental therapies being investigated for patients with ARDS is the use of inhaled nitric oxide. Nitric oxide is an endothelium-derived relaxing factor that produces relaxation of the vascular smooth muscle. When inhaled, nitric oxide decreases the shunt fraction by redistributing blood flow from poorly ventilated areas to well-ventilated areas of lung. The effect of nitric oxide is to decrease pulmonary artery pressures, decrease pulmonary vascular resistance, and increase \( P_{ao2} \) by increasing blood flow to well-ventilated areas. The use of nitric oxide in the management of acute lung injury is being extensively investigated in the literature and is still considered experimental.

Nitric oxide is delivered in doses of 5 to 80 ppm. Using dedicated ventilators, nitric oxide is blended with nitrogen and bled into the air outlet of the ventilator. Because they are bled into the air outlet, the set \( FIO_2 \) does not equal the delivered \( FIO_2 \). Thus, close collaboration with the respiratory therapist is key to ensure proper dosing. The expired gas is scavenged in a cylinder to eliminate nitric oxide and nitrogen from the environment to make it safe for the caregivers.

When suctioning a patient receiving nitric oxide, the use of in-line suction is imperative to prevent the escape of exhaled gases into the air. When suctioning, hand ventilation should not be used to preoxygenate because it interrupts the flow of the nitric oxide and allows for the escape of exhaled gases. Close monitoring of pulmonary artery pressures and intrapulmonary shunt assists in assessing the efficacy of the nitric oxide therapy.

Although significant investigation is in progress, no studies that define the efficacy of nitric oxide on outcomes are available. Some questions that remain to be answered include:

- When is it best to initiate therapy?
- What is the proper dosing?
- How is it best weaned up and down?
- What long-term effects does it produce?
- What immediate physiologic effects are seen at the bedside?

**SUMMARY**

Acute respiratory distress syndrome is a complex clinical syndrome of respiratory failure that presents a challenge to every critical care team. Since the first clear description by Ashbaugh et al. more than 30 years ago, much has been learned about the pathophysiologic process that occurs within the lungs after they suffer either a direct or indirect injury. Unfortunately, little success has been achieved in improving outcomes; however, hope is on the horizon. Current research evaluating optimal ventilator management, ECMO, the use of inhaled nitric oxide, and other experimental management strategies will hopefully combine to produce improved outcomes.
ACKNOWLEDGMENTS

The author wishes to acknowledge the support and mentorship of Sarah Kagan, PhD, RN, in the preparation of this manuscript and the dedication of the Rhoads 5 Surgical Critical Care staff for their care of these very complex patients.

REFERENCES

1. Aherns TS, Beattie S, Niemhaus T: Experimental therapies to support the failing lung. AACN Clinical Issues 7:507, 1996
2. Albert RK: The prone position in acute respiratory distress syndrome: Where are we, and where do we go from here? Crit Care Med 25:1453, 1997
3. Amato MBP, Barbas CSV, Medeiros DM, et al: Effect of a protective ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 338:347, 1998
4. Anderson H, Steimle C, Shapiro M, et al: Extracorporeal life support for adult cardiopulmonary failure. Surgery 114:116, 1993
5. Anderson HL, Bartlett RH: Extracorporeal membrane oxygenation and carbon dioxide elimination. In Rippe JM, Curley FJ, Herd SO (eds): Procedures and Techniques in Intensive Care Medicine. Boston, Brown, Little & Co, 1995
6. Ashbaugh DG, Bigelow DB, Petty TL: Acute respiratory distress in adults. Lancet 2:319, 1967
7. Basham KR, Vollman KM, Miller AC: To everything turn, turn, turn... An overview of continuous lateral rotational therapy. Respiratory Care Clinics of North America 3:109, 1997
8. Burns SM: Understanding, applying, and evaluating pressure modes of ventilation. AACCN Clinical Issues 7:495, 1996
9. Chapman MJ: Adult respiratory distress syndrome: An update. Anaesth Intensive Care 22:255, 1994
10. Chillcott S, Sheridan PS: ECO2R2: An experimental approach to treating ARDS. Crit Care Nurse October: 31–36, 1995
11. Goff W, Orgura H: Inhaled nitric oxide in acute lung disease. New Horiz 3:73, 1995
12. Cottingham CA, Habashi NM: Extracorporeal lung assist in the adult trauma patient. AACN Clinical Issues 6:229, 1995
13. Dirkes D, Dickinson S, Valentine J: Acute respiratory failure and ECMO. Crit Care Nurs October: 39–47, 1992
14. Dirkes S, Dickinson S, Valentine J: Acute respiratory distress syndrome. Arch Intern Med 156:29, 1996
15. Gattinoni L, Pesenti A, Mascheroni D, et al: Low-frequency positive-pressure ventilation with extracorporeal CO2 removal in severe acute respiratory failure. JAMA 32:508–510, 1986
16. Gentilello L, Thompson DA, Tonnesen AS, et al: Effect of a rotating bed on the incidence of pulmonary complications in critically ill patients. Crit Care Med 16:783, 1988
17. Gottlieb JE: Breathing and gas exchange. In Kinney MR, Packa DR, Dunbar SB (eds): AACN’s Clinical Reference for Critical Care Nursing, ed 2. New York, McGraw-Hill, 1988, p 160
18. Hamm J: Challenging diagnosis: Adult respiratory distress syndrome. Crit Care Nurs October: 46, 1995
19. Hickling MB, Walsh J, Henderson S, et al: Low mortality rate in adult respiratory distress syndrome using low volume, pressure-limited ventilation with permissive hypercapnia: A prospective study. Crit Care Med 22:1568, 1994
20. Hudson LD, Steinberg KP: Acute respiratory distress syndrome: Critical features, management, and outcome. In Fishman AP, Elias JA, Fishman JA, et al (eds): Fishman’s Pulmonary Diseases and Disorders, ed 3. New York, McGraw-Hill, 1998, p 2549
21. Humphrey HJ, Hall J, Snajer JJ, et al: Improved survival following pulmonary capillary wedge pressure reduction in patients with ARDS. Chest 97:1176, 1990
22. Kanto WP, Shapiro MB: An introduction to extracorporeal life support. In Zwischenberger JB, Bartlett RH (eds): ECMO: Extracorporeal Cardiopulmonary Support in Critical Care. Ann Arbor, MI, Extracorporeal Life Support Organization, 1995
23. Kollef MH, Schuster DP: Medical progress: The acute respiratory distress syndrome. N Engl J Med 332:27, 1995
24. Langer M, Mascheroni D, Marcolin R, et al: The prone position in ARDS patients. Chest 96:103, 1988
25. Lu J: Acute lung injury and acute respiratory distress syndrome. Crit Care Med 26:369, 1998
26. Lasater-erhard M: The effect of patient position on arterial oxygen saturation. Crit Care Nurs October: 31, 1995
27. Marinelli WA, Ingbar DH: Diagnosis and management of acute lung injury. Clin Chest Med 15:517, 1994
28. Minardi JJ: New options for the ventilatory management of acute lung injury. New Horiz 1:489, 1993
29. Minardi JJ: Mechanical ventilation: Physiological considerations and newer ventilatory techniques. In Fishman AP, Elias JA, Fishman JA, et al (eds): Fishman’s Pulmonary Diseases and Disorders, ed 3. New York, McGraw-Hill, 1998, p 2709
30. Matus VW, Glennon SA: Respiratory disorders. In Kinney MR, Packa DR, Dunbar SB (eds): AACN’s Clinical Reference for Critical Care Nursing, ed 2. New York, McGraw-Hill, 1988, p 774
31. McIntyre RC, Moore FA, Moore EE, et al: Inhaled nitric oxide variably improves oxygenation and pulmonary hypertension in patients with acute respiratory distress syndrome. J Trauma 39:418, 1995
32. Murre M, Martling CR, Lindahl SG: Demonstic effects on oxygenation in patients with severe acute lung insufficiency treated in the prone position. Crit Care Med 25:1539, 1997
33. Pappert D, Rossaint R, Slama L, et al: Influence of positioning on ventilation-perfusion relationships in severe adult respiratory distress syndrome. Chest 106:1511, 1994
37. Pepe PE, Potkin RT, Reus DH, et al: Clinical predictors of adult respiratory distress syndrome. Am J Surg 140:814, 1982
38. Rinaldo JE, Christman JW: Acute respiratory distress syndrome: Pathogenesis. In Fishman AP, Elias JA, Fishman JA, et al (eds): Fishman’s Pulmonary Diseases and Disorders, ed 3. New York, McGraw-Hill, 1998, p 2537
39. Roberts SL: High permeability pulmonary edema: Nursing assessment, diagnosis and interventions. Heart Lung 19:287, 1990
40. Rossaint R, Gerlach H, Schmidt-Ruhnke H, et al: Efficacy of inhaled nitric oxide in patients with severe ARDS. Chest 107:1107, 1995
41. Safcsak K: High-level positive end expiratory pressure management in the surgical patient with acute respiratory distress syndrome. AACN Clinical Issues 7:482, 1996
42. Schuller D, Mitchell JP, Calandrino FS, et al: Fluid balance during pulmonary edema: Is fluid gain a marker or cause of poor outcome? Chest 100:1068, 1991
43. Shoemaker WC, Appel PL, Bishop MH: Temporal patterns of blood volume, hemodynamics and oxygen transport in pathogenesis and therapy of postoperative ARDS. New Horiz 1:522, 1993
44. Stewart TE, Meide MO, Cook DJ, et al: Evaluation of a ventilation strategy to prevent barotrauma in patients at high risk for acute respiratory distress syndrome. N Engl J Med 338:355, 1998
45. Sumner WR, Curry P, Haponik EF, et al: Continuous mechanical turning of intensive care patients shortens length of stay in some diagnostic related groups. J Crit Care 4:45, 1989
46. Taylor RW, Norwood SH: The adult respiratory distress syndrome. In Cvietta JM, Taylor RW, Kirby RR (eds): Critical Care, ed 2. Philadelphia, JB Lippincott, 1992
47. Trotter SJ, Taylor RW: Adult respiratory distress syndrome. In Textbook of Critical Care (ed. 3). Philadelphia, WB Saunders. 1995
48. Varon J, Wenker OC: The acute respiratory distress syndrome: Myths and controversies. The Internet Journal of Emergency and Intensive Care Medicine 1N1:1996 http://www.ispub.com/journals/IJEICM/volIN1/ards.htm
49. Vaughan P, Brooks C: Adult respiratory distress syndrome: A complication of shock. Crit Care Nurs Clin North Am 2:235–253, 1990
50. Vollman KM: Adult respiratory distress syndrome: Mediators on the run. Crit Care Nurs Clin North Am 6:341–358, 1994
51. Vollman KM: Prone positioning for the ARDS patient. Dimensions in Critical Care Nursing 16:84–192, 1997
52. Whiteman K, Nachtmann L, Kramer D, et al: Effects of continuous lateral rotation therapy on pulmonary complications in liver transplant patients. Am J Crit Care 4:133–139, 1995
53. Zapol WM, Snider MT, Hill JD, et al: Extracorporeal membrane oxygenation in severe acute respiratory failure: A randomized prospective study. JAMA 242:2193–2196, 1979

Address reprint requests to JoAnne K. Phillips, RN, MSN, CCRN Rhoads 5, Surgical Critical Care Unit Hospital of the University of Pennsylvania 3400 Spruce Street Philadelphia, PA 19104