CHAPTER 1

Acute Respiratory Distress Syndrome (ARDS)

CHAPTER OUTLINE

DEFINE
- Define acute lung injury/acute respiratory distress syndrome (ALI/ARDS)
- Discuss whom ALI/ARDS affects

DESCRIBE
- Describe the clinical presentation of ALI/ARDS
- Describe the etiology of ALI/ARDS

DISTINGUISH
- Distinguish ALI/ARDS from congestive heart failure (CHF)
- Distinguish the phases of ALI/ARDS
- Distinguish the phases illustrated in this clinical case review

RESEARCH
- Relevant research on ALI/ARDS

TREATMENT
- Treatment options in the care of ALI/ARDS patients
- Respiratory therapist role in the management of ALI/ARDS

KEY TERMS

Acute lung injury (ALI)
Acute respiratory distress syndrome (ARDS)
Extracorporeal membrane oxygenation (ECMO)
Heliox administration
High-frequency oscillatory ventilation
Infant respiratory distress syndrome
Inhaled nitric oxide
Lung protective strategy
Mechanical ventilator
Partial liquid ventilation
Prone positioning
Recruitment maneuver

DEFINE

Acute lung injury and acute respiratory distress syndrome (ALI and ARDS) is a syndrome marked by severe lung injury that causes an acute hypoxemia respiratory failure requiring high levels of oxygen and positive end-expiratory airway pressure (PEEP) therapy. Egan's *Fundamentals of Respiratory Care* makes a distinction between ALI and ARDS: the latter is classified as more serious, leading to other organ failures.[1,2,3] Khemani and colleagues suggest the definition used to establish ARDS in adults is valid in establishing the diagnosis in children.[4] According to Pilbeam and Cairo, approximately 75% of all ALI cases develop into ARDS.[2] **Figure 1-1** highlights recommended criteria for ALI and ARDS.

The American European Consensus Conference (AECC), who was charged with the development of a standardized definition of ARDS, officially defined it as follows:[5] "A syndrome of inflammation and increasing permeability that is associated with a constellation of clinical, radiologic, and physiologic abnormalities that cannot be explained by, but may co-

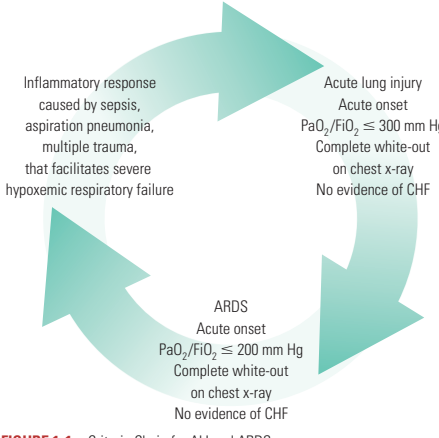

FIGURE 1-1 Criteria Chain for ALI and ARDS

exist with, left atrial or pulmonary capillary hypertension" and "is associated most often with sepsis syndrome, aspirations, primary pneumonia, or multiple trauma and less commonly with cardiopulmonary bypass, multiple transfusion, fat embolism, pancreatitis and others."

DESCRIBE

Clinical presentation of ARDS is characterized as a severe ventilation perfusion mismatch that leads to significant respiratory hypoxemic failure. ALI/ARDS can present in any number of ways. What follows are a few examples of risk factors common in children with ARDS. This list represents only a snapshot of the many causes of ARDS.

- Pneumonia
- Aspiration pneumonia
- Shock
- Multiple trauma
- Head injury
- Near drowning
- Extensive burns
- Oxygen toxicity
- Narcotic drug overdose
- Pulmonary contusion

Clinical Signs

- Increase in respiratory rate
- Retractions
- Dyspnea
- Pulmonary edema
- Bilateral crackles noted on auscultation
- Respiratory alkalosis secondary to hyperventilation
- Worsening arterial blood gases as the disease progressively leads to respiratory insufficiency
- No response to oxygen therapy with worsening lung compliance
- Chest x-ray showing diffuse bilateral infiltrates (complete whiteout)

DISTINGUISH

Care must be made to distinguish ARDS from congestive heart failure (CHF) because signs and symptoms of ARDS can be similar in patients with CHF.

Signs of CHF include the following:

- History consistent with heart failure
- Enlarged heart on chest x-ray
- Pleural effusion
- Pulmonary capillary wedge pressure of greater than 18 mm Hg[1]

Clinical Case Review

Good clinical cases are excellent models to demonstrate the phases of ARDS. This case demonstrates the four phases of ARDS in a child with a suspected chemical toxin inhalation. A 12-year-old boy was admitted to the pediatric intensive care unit with a high fever and uncontrollable coughing, as reported by the child's mother. Prior to these events the boy had been healthy. Mother reports that her son went to play at a park near their home. She noticed that across the street from the park a demolition construction crew was working. The crew was removing an old housing project that had been abandoned. Mother said she cautioned her son to stay clear of the construction crew and then left her son in the park to play while she returned home. An hour later the son appeared at home, but immediately went to his room. The mother thought it was odd that her son would go to his room because he is very active. Mother followed to her son's room to find him in bed complaining of being tired. Mother felt his head, which appeared warmer than usual, so she took his temperature. The result was 39.9 centigrade. Mother immediately rushed her son to the emergency room at their nearby hospital. During the ride to the hospital the son complained that he was having a hard time breathing. Mother could hear her son in the back seat of the car having what she described as a "coughing fit." Mother made attempts to calm her son during the ride, but her only hope was to get her son to the hospital as quickly as possible. Mother reports no history of asthma or cardiac disease

with her son or anyone in the family. Apart from the above history, there were no other significant health issues with her son.

Initial Vital Signs upon Arrival to the Emergency Room

Phase 1

- 4 hours since the child was in the park
- 12-year-old boy appropriate height and weight for his age
- Observed shortness of breath, respiratory rate: 30 to 35 breaths per minute
- Heart rate: 120 to 130 bpm
- SaO_2: 95% on room air
- ABG results: relatively normal with PaO_2 84 mm Hg and $PaCO_2$ 37 mm Hg
- Retractions observed
- No nasal flaring
- Breath sounds: diminished airflow throughout lung fields
- Capillary refill: less than 3 seconds
- Chest x-ray appears normal
- Child still able to speak, although sentences are slightly choppy

From this assessment, it appears that this 12-year-old is in phase 1 of ARDS. Kenneth Whitaker, in his pediatric textbook, divides ARDS into four phases, in which phase 1 occurs within 1 to 12 hours of the initial injury.[6] It is not clear from the child's history as to the direct cause, but one could surmise that the child inhaled chemical toxins while in close proximity to an old building being demolished. In phase 1 of ARDS, blood gas values and chest x-ray may look normal, yet clinically the patient may show evidence of inadequate ventilation and gas exchange.

Respiratory Therapist Initial Response

- 100% nonrebreather mask to deliver as close to 100% FiO_2 as possible
- Close monitoring for signs of increasing respiratory distress
- Preparation for possible intubation

Phase 2

The child has progressed to severe respiratory distress with the following parameters:

- Respiratory rate: 40 to 50 breaths per minute
- Heart rate: 120 to 130 bpm
- Breath sounds: crackles throughout
- Chest x-ray: some bilateral infiltrates
- Arterial blood gas shows a respiratory alkalosis with a mild hypoxemia (pH 7.48 $PaCO_2$ 32, PaO_2 68 HCO_3 26 on 100% nonrebreather mask)

Phase 2 occurs 12 to 24 hours after the initial lung injury, and this is really the time to begin aggressive treatment.[6] At this point a decision is made to intubate this child. Although the arterial blood gas shows a respiratory alkalosis with a mild hypoxemia, it is in the child's best interest that the intubation is done now. It is not surprising that a few hours before the decision to intubate, the child appeared to be in phase 3 of ARDS.[6] Understanding and interpreting arterial blood gases is critical in the management of children with ALI/ARDS. For example, the above blood gas shows a respiratory alkalosis with mild hypoxemia, which is evident of a child hyperventilating secondary to maintaining adequate gas exchange. When this child shows signs of fatigue, respiratory acidosis becomes evident, which is a direct correlation to increasing carbon dioxide production secondary to decreased or ineffective respiratory efforts. Hypercarbia respiratory failure, acute pH less than 7.25, and acute $PaCO_2$ greater than 55 is the standard used in the decision to intubate. As we will soon learn, this child has met the criteria for intubation. An in-depth discussion of arterial blood gas interpretation is beyond the scope of this guide book; however, there are a number of excellent respiratory books with chapters devoted to this topic. Egan's *Fundamentals of Respiratory Care*, the chapter on arterial blood gas, is a good place to start.[1]

Phase 3

- The boy can hardly speak and is breathing very shallowly.
- He is becoming more lethargic.

- His arterial blood gas shows a respiratory acidosis with now a moderate hypoxemia.

Respiratory Therapist Follow-Up Response

Respiratory therapist recommends intubation.
Child is intubated with a #6 endotracheal tube. Chest x-ray showed endotracheal tube placement in good position.
Chest x-ray also shows lungs with noticeable diffuse bilateral infiltrates. This concurs with phase 3 of ARDS:

- Severe respiratory acidosis
- Severe hypoxemia
- Evidence of diffuse bilateral infiltrates

A sample of ventilator settings:
Mode: Assist control
Rate: 16
V_t: 4 to 6 ml/kg based on ARDSnet protocol
FiO_2 initial: 100%
PEEP: Titrate PEEP levels to maintain the lowest PEEP to keep lungs open at the end of exhalation while assuring an acceptable PaO_2

See **Table 1-1** for initial ventilator settings.

Considering all aspects of ARDS, it is necessary to be on the alert for changes in airway resistance and lung compliance while being ventilated. Avoid air trapping and auto-PEEP as much as possible. During the child's stay in the PICU, there were many ventilator changes as a result of worsening ventilatory failure, conclusive evidence of phase 4 ARDS.

Phase 4

- Worsening respiratory failure
- Worsening arterial blood gases
- Multiple organ failure—the child now has acute renal failure
- Significant fibrosis of the lung parenchyma
- Severe ventilation and perfusion mismatch
- Has been on the ventilator for more than 2 weeks

TABLE 1-1 Suggested Initial Settings for Mechanical Ventilation

Mode	Assist control SIMV with pressure control and pressure support APRV (These are three examples—your ventilator may have other modes that will work equally as well.)
Rate	12 to 20 breaths/minute
Tidal volume	4 to 6 ml/kg or 5 to 7 ml/kg based on ideal body weight and your hospital specific protocol[7,8]
Oxygen	FiO_2 to keep SaO_2 greater than 90%
PEEP	Titrate PEEP levels to maintain the lowest PEEP level to keep lungs open at the end of exhalation while assuring an acceptable PaO_2 (see Table 1-4).
Flow	Some ventilators may automatically adjust flow; if not, then flow should be adequate to meet the patient inspiratory flow demand.
I:E ratio	1:2 If using APRV, the I:E ratio maybe inversed.
Inspiratory time	0.8 to 1 second when using either AC or PC. This may be different if using APRV.
Trigger or sensitivity	Flow trigger 1 to 3 L/min or pressure trigger 0.5 cm to 2 cm H_2O

In just a little under 48 hours, significant changes have occurred to this child's lung tissue, making the lungs stiffer and causing a major ventilation and perfusion mismatch. So no matter how you look at it, ARDS is a force to be reckoned with.

It is most important that the respiratory therapist have an understanding of the big picture of ARDS. This understanding is what makes a respiratory therapist invaluable to the medical team.

RESEARCH

Acute respiratory distress syndrome (ARDS), as the literature points out, is a subset of acute lung injury (ALI). For the purpose of this discussion, ALI/ARDS will be used interchangeably to mean one and the same. For all intents, we should really call it "Devastation, Devastation, Devastation,"

for that is what we see when patients present with ALI/ARDS. Historically, ALI/ARDS has undergone numerous name changes: adult respiratory distress syndrome was one; however, inasmuch as there have been name changes, the research clearly articulates that ARDS has not been selective to adults but to anyone who has a set of lungs. One research study made a distinction between the adult version and the infant version of ARDS. This chapter will focus on the research of children over 1 year old, and Chapter 2 will deal exclusively with infant respiratory distress syndrome of children younger than 1 year of age. Just as there will be overlapping between these two chapters, there will be distinct differences, particularly in the area of treatment.

There is much research about ALI/ARDS because, according to the National Heart Lung Blood Institute (NHLBI), the condition affects more than 150,000 persons in the United States annually.[3] Other researchers argue that the number is much lower than 150,000: more like 20,000 to 30,000 cases per year.[1] Mortality rate is still high, despite the advancement made in the treatment of the disease, and death is still projected at 30% to 40% owing to multiple organ failure.[1,3,5,6] ARDS is believed to be a public health crisis costing the United States millions of healthcare dollars.[5] Consequently, there is a great interest to fund research to find a cure for ARDS.

Interestingly enough, ARDS was identified some 100 years ago; yet, it would be 50 years before we would recognize ARDS as we know it today. Recognition of ARDS was brought into focus around the same time mechanical ventilators became popular and the establishment of intensive care units.[9] In 1967, a major study published in *Lancet* by Ashbaugh et al. described the clinical appearance of *adult respiratory distress syndrome*. The authors concluded that ARDS was initiated by a number of unrelated events that caused the lungs to behave abnormally. They cited such examples as gastric aspiration, sepsis, blunt trauma, and near drowning, to name a few.[2,5] You can find the American European Consensus Conference (AECC) standardized definition of ARDS on page 2 in this book.[5]

Additionally, ARDS was classified as a subset of acute lung injury, in which both conditions are acute in onset: low arterial hypoxemia that does not respond to oxygen therapy alone, and chest x-rays that show

diffuse infiltrates.[1,2,5] In addition, Miles et al. further define ALI as a PaO_2/FiO_2 ratio of 300, in which ARDS' ratio is 200.[1,2,10] Khemani and colleagues agree that the use of the P/F ratio is adequate in defining ARDS and ALI; however, their research showed that using SpO_2/FiO_2 may also be a reliable method of identifying children with lung injury.[4] One thing is clear: ARDS has been studied at length from a variety of perspectives, and yet no cure has been introduced. Most of the research has focused on supportive care to minimize the damage to the lungs, thereby improving overall outcomes. Although patients with ARDS are placed on mechanical ventilators, early research demonstrated that, in fact, the mechanical ventilator may have exacerbated an already injured lung. A number of studies were done to show the effects of various ventilator parameters on lung tissue. In 1994, the ARDS Clinical Research Network (ARDSnet) of the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH), conducted a clinical trial comparing various lung protective strategies.[10,11] Low tidal volume (6 ml/kg) was compared to conventional tidal volume or high tidal volume (12 ml/kg). They hypothesized that those in the low tidal volume group would have better outcomes than those in the high tidal volume group. The study showed a significant reduction in mortality for the low tidal volume group. ARDSnet further demonstrated that with the low tidal volume group, there were fewer ventilator days, less multiple organ failure, and less circulating inflammatory markers frequently seen in patients with ARDS.[10,11] Whereas the ARDSnet showed success, this was just the beginning of similar studies set out to either confirm or refute the ARDSnet findings. Although the ARDSnet population included mostly adults, Hanson and Flori agree that applying the low-tidal-volume strategy to children with acute lung injury was appropriate because the ARDSnet has proven a successful strategy in several large, multicenter clinical trials.[12]

A second very important study from the ARDSnet was the use of positive end-expiratory pressure (PEEP) as an alveoli recruitment maneuver.[11] PEEP has been the gold standard used to recruit alveoli, decrease oxygen requirement, and improve lung compliance. In 80 of the patients assigned to the high-PEEP group, recruitment maneuvers were performed. These patients were placed on high PEEP of 35 to 40 cm H_2O

for 30-second periods. The researchers found only modest benefit to improving oxygenation while performing the recruitment maneuver. Thus recruitment maneuvers were stopped. Although the ARDSnet did not include high PEEP as a part of their protocol, the researchers cautioned that high PEEP should be reserved as a recruitment maneuver for those patients with a serious oxygen defect that is not responding to current oxygen therapy. Whereas the ARDSnet found only modest benefit, Meade et al. successfully conducted a clinical trial in which they studied 983 ALI/ARDS patients from 2000 to 2006.[13] Their protocol, although similar to the protocol used in ARDSnet, used low tidal volumes, recruitment maneuvers, and high PEEP to recruit and open the lung. Unlike the ARDSnet, their recruitment maneuver was started with PEEP of 20 cm H_2O, routinely done 4 times a day until the patient was weaned to an FiO_2 of 40% or less.[13] This group maintained a control group, which followed the ARDSnet protocol, and the experimental group, which was subject to the higher PEEP levels. Their results suggest that there was more hypoxemia and increased FiO_2 in the control group, similar tidal volumes in both groups, and higher plateau pressures in the experimental group. Overall, they found more similarities than differences between the groups because the open lung ventilation strategy resulted in no greater mortality than that of the control group. The authors acknowledged there were limitations to this clinical trial: it was difficult to tell whether it was the effect of the higher PEEP, the recruitment maneuvers, or higher plateau pressure that made an impact on mortality. They concluded their findings with the observation of using a multifaceted open lung-protective ventilation strategy as an alternative to the current established low-tidal-volume ventilation strategy.[11] Based on their findings, they support the use of higher PEEP levels. The authors readily admit that success of the protocol was owed in part to those clinicians "increasingly comfortable with higher levels of PEEP."

Currently, there are more than 100 clinical trials at various stages funded by the NHLBI to answer these four basic questions about ARDS: (1) What initiated the lung injury? (2) What mediates progression of ongoing lung injury? (3) What causes persistent fibrosis and pulmonary hypertension? (4) What mediates the propagation of injury from the

lung to other organs."[5,10] Much of the research has focused on ventilator care; however, a few studies worth noting have directed our attention to nonventilator strategies for managing ARDS: (1) surfactant replacement therapy, (2) prone position, and (3) inhaled nitric oxide.

The research is clear regarding the benefit of surfactant replacement therapy (SRT) in the neonate, an infant born before 37 weeks, who lack mature surfactant. Moller et al. suggest in their research that the use of bovine surfactant administered intratracheally with continuous mechanical ventilation showed improvement in oxygenation in older children; however, this study found improvement in patients who did not have pneumonia and already had a P/F ratio that was greater than 65.[14]

Although surfactant therapy has proven successful for the neonate with infant respiratory distress syndrome, meconium aspiration syndrome, and other conditions comparable to ARDS, there is a need for randomized clinical trials in the pediatric age group evaluating administration of SRT for the treatment of refractory hypoxemia. Prone position has been shown in the adult population to improve lung compliance and promote better gas exchange. Relvas and colleagues report that in pediatric patients with ARDS, prone position for 18 to 24 hours a day showed significant improvement in oxygenation compared to prone position for less than 12 hours per day.[15] Prone position has been shown to promote oxygenation in the following ways:

- Better diaphragmatic movement
- Recruitment of formerly collapsed dependent lung regions
- Rerouting pulmonary blood flow, enhanced drainage of airway secretions
- Increased negative pleural pressure[15]

Finally, the use of inhaled nitric oxide in children with ARDS may show promise in the treatment of refractory hypoxemia. Inhaled nitric oxide is an endogenous endothelial-derived mediator that causes smooth muscle relaxation.[16] Baldauf et al. were not convinced of the benefits of iNO because studies of its use were small and not clinically impressive. The aim of their study was to develop an analytic tool that would validate the responsiveness to the use of iNO in children. Nineteen children were enrolled in their study. Controlling for known variables, they

observed the change in mean pulmonary arterial pressure and P/F ratio as a measurement of significance. They report an improvement in both parameters.[16] This study concludes that when clinicians report observable improvement in oxygenation with the administration of iNO, it is reported using an instrument that would validate their findings and these are not purely speculative or anecdotal comments.

Although there are more unanswered questions than answered ones, it is comforting to know that research is ongoing and that soon answers may be forthcoming. But until then, we concentrate on supportive care. There are a number of treatment options that are used for ALI/ARDS patients. The next section will discuss how respiratory therapists play an integral role in the management of patients with ARDS.

TREATMENT

The key to improved mortality and reducing morbidity is early recognition of a child with ALI or ARDS. Early recognition results in early treatment geared toward improving outcomes. The role of the respiratory therapist will be many: from the emergency room to the pediatric intensive care unit. Because ventilation and oxygenation are overriding factors in the management of ARDS patient, the job of the respiratory therapist will be to help develop a plan that will promote adequate ventilation while improving oxygenation. Believe me, this is no small feat. A well-thought-out management plan for patients with ARDS includes the entire medical team. There are a number of approved therapies for the treatment of ARDS. **Table 1-2** highlights some of the approved modalities that a respiratory therapist would use to manage a child with ARDS. Following this chart is a detailed discussion of the modalities and illustrations of the actual equipment setup.

Discussion of Each Treatment Modality

Conventional Mechanical Ventilation Recommendations from the ARDSnet for mechanical ventilation suggest a lung-protective strategy that employs low tidal volumes, higher rates, and an FiO_2/PEEP combination that will facilitate adequate oxygenation. Although there is ongoing debate with regard to the ARDSnet findings, it remains the standard of

TABLE 1-2 Treatment Options for the ARDS

Type of Therapy	Application
Conventional ventilation Mode of ventilation Assist control	ARDSnet suggests tidal volume between 5 to 7 ml per kg of ideal body weight.[7,8] It might be appropriate in your PICU to use 4 to 6 ml/kg. The protocol established in your PICU will dictate. Assist control FiO_2 to keep SaO_2 greater than 92% Optimal PEEP: see next section. Ventilator rate 12–20 using your arterial blood gas as your guide. Some ventilators are equipped with end tidal CO2 manometer, which is useful in evaluating exhaled CO2.
Optimal level of PEEP	Titrate PEEP levels to maintain the lowest PEEP level to keep lungs open at the end of exhalation while assuring an acceptable PaO_2.
Pressure control ventilation (PCV): consider this mode if you are unable to control the peak inspiratory pressure using volume control mode as described above.	Maximum peak inspiratory pressure: a starting point should be the plateau pressure from previous mode. The goal is to remain below 30 cm H_20; however, 30 to 35 cm H_2O may be required to maintain adequate ventilation. Caution: monitor closely for changes in hemodynamic stability because the higher the peak pressure, the more likely to impede venous return.
Airway pressure release ventilation (APRV)	Used most often in adult ventilation when either assist control or pressure control has failed. This mode of ventilation requires the patient to breathe spontaneously at two different pressure levels: a high pressure and a low pressure. Frequency is set by setting the high time and low time.
High-frequency oscillatory ventilation (HFOV)	HFOV uses smaller tidal volumes (less than 5 ml/kg), fewer variable airway pressures, and rates up to 300 breaths per minute.
Prone positioning	Placing a patient on his or her stomach in a head-down position has been shown to improve the ventilation perfusion mismatch so often seen in ARDS patients.
Extracorporeal membrane oxygenation (ECMO)	This is a technique developed that is similar to the heart-lung bypass machine used in adults. In children it has been used as a rescue therapy in the early phase of ARDS. This therapy is used most often with patients who have life-threatening ARDS when other therapies designed to improve oxygenation have failed.
Inhaled nitric oxide (iNO)	Nitric oxide is a colorless, odorless gas that was found to be a selective pulmonary vasodilator in patients with pulmonary hypertension.
Heliox administration	The literature has demonstrated that heliox has shown to improve oxygenation when used in combination with HFOV for patients with ARDS.
Partial liquid ventilation (PLV)	Perfluorocarbon has the ability to dissolve large volumes of oxygen and CO_2 at atmospheric pressure, thereby reducing surface tension in lungs that are surfactant-deficient.

care at this time. The pinnacle of the ARDSnet protocol is the use of low tidal volumes (6 ml/kg of predicted body weight). The selection of the tidal volume can be done based on the patient's actual weight.[7,8] The selection of your ventilator setting is not under debate: the ultimate goal is to choose a volume that is appropriate, delivers adequate chest rise, avoids alveolar overdistention, and allows a chest x-ray that demonstrates no further harm to the lung tissue based on your ventilator settings. Keep in mind that although the use of the low tidal volume strategy is a lung protective strategy, some patients' arterial blood gas will inevitably show a respiratory acidosis. The use of this strategy is called permissive hypercapnia, and in some patients pH levels as low as 7.10 to 7.20 have been tolerated.[17] Permissive hypercapnia is tolerated well in young people and those with few cardiovascular abnormalities.

As a subset to conventional ventilation, airway pressure release ventilation (APRV) has been suggested as a mode of ventilation that has promise in the treatment of patients with ALI/ARDS. This mode allows a patient to breathe spontaneously at two separate pressure levels. Some authors suggest that APRV is similar to breathing at two continuous positive airway pressures (CPAP) in which the higher level of CPAP helps support the tidal volume while the subsequent drop to the lower CPAP level acts to reduce the mean airway pressure. The frequency is controlled by time: the expiratory time is short, which aids improved functional residual capacity while promoting an inverse inspiratory and expiratory ratio. One thing to keep in mind—this mode is pressure augmentation, and so as with all pressure generated ventilation, similar hazards exist. The advantages of this mode are decreased need for sedation, patient ability to control spontaneous ventilation, and overall better patient-ventilator synchrony. **Figure 1-2** shows two different types of conventional mechanical ventilator with APRV capabilities.

Although pressure breathing has significant benefits in ALI/ARDS ventilator management, PEEP therapy has made the most gains. This was evident in the ARDSnet study and continues to this day in clinical practice, so a word about the importance of PEEP is in order. Although PEEP

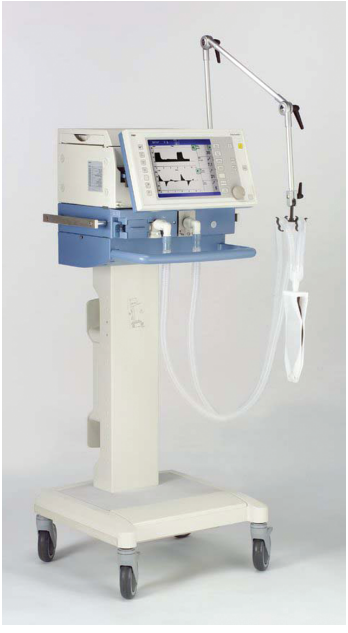

FIGURE 1-2 Conventional ventilator with APRV capabilities

has its drawbacks, the following are some of the benefits for ALI/ARDS patients using PEEP:

- Improved intrapulmonary shunting
- Improved functional residual capacity
- Improved pulmonary compliance
- Improved dead-space ventilation ratio
- Improved work of breathing

Understanding PEEP will crystallize the lung recruitment maneuver. Priestly and Helfaer describes a recruitment maneuver as a sustained increase in airway pressure with the goal of opening collapsed lung tissue.[18] Recruitment is of particular importance when using low tidal volumes and low levels of PEEP. The ARDSnet proposed that very high levels of PEEP be used over 30 to 40 seconds, whereas other researchers proposed that slightly lower PEEP levels be used for lung recruitment. Facility-specific protocol on lung recruitment maneuver will be the best guide for the respiratory therapist when suggesting the need for lung recruitment.

High-Frequency Oscillatory Ventilation (HFOV) High-frequency oscillatory ventilation (HFOV; see **Figure 1-3**) has been shown to reduce mortality and improve oxygenation in ARDS patients if used early in the disease process. The operative words here are "used early." This mode has been demonstrated in the pediatric patient and is currently approved by the Food and Drug Administration (FDA) as an alternative to conventional ventilation. According to William Miles and his group, HFOV has been studied in infants comparing HFOV and conventional ventilation (CV), and results show improvement in oxygenation, reduced ventila-

TABLE 1-3 PEEP/ FiO_2 Combination Used in the ARDSnet Mechanical Ventilation Protocol

FiO_2	PEEP
0.3	5
0.4	5–8
0.5	8–10
0.6	10
0.7	10–14
0.8	14
0.9	14–18
1.0	18–24

Note: Settings are from the ARDSnet trial and indicate the required FiO_2 to keep oxygen saturation above 90%. This table is important because it demonstrates titrating of PEEP and FiO_2 up or down to get the desired PaO_2. This is best done in connection with a PEEP trial in which the ideal PEEP will be one that has the best PaO_2 in relation to $PaCO_2$, compliance, cardiac output, mean arterial pressure, and mean pulmonary artery pressure.

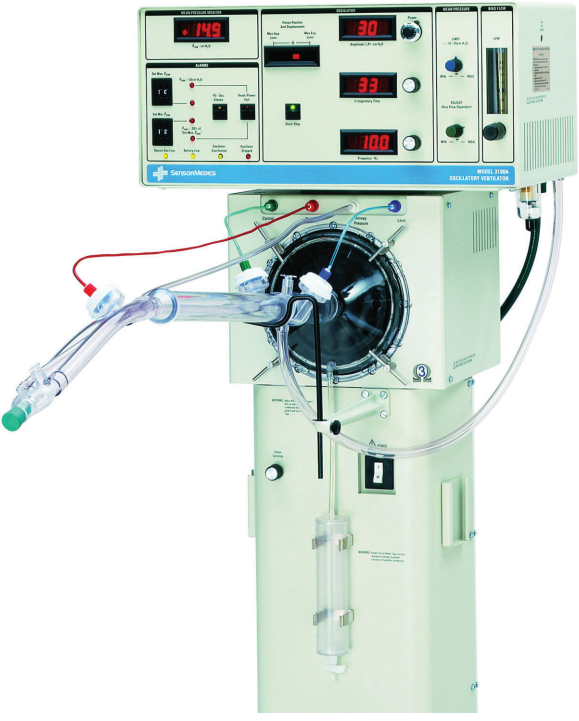

FIGURE 1-3 HFOV

tor-associated lung injury, decrease in mortality, and fewer mechanical ventilator days.[10]

Although HFOV has been studied extensively in infants and children, it has not garnered the attention in the adult population with ARDS. In fact, there have been only a few randomized control studies as reported by Miles and others. The clinical trials that were reviewed did show that HFOV is a safe and effective mode of ventilation for the treatment of ARDS in adults.[10]

How Does HFOV Operate? HFOV uses smaller tidal volumes and less variable airway pressures. This prevents the constant opening and closing shearing forces of lung tissue as seen with conventional ventilation. HFOV is designed to keep the alveoli in an open state, so as alveoli are opened and remain open, the gas moves around the lung tissue seeking to open as many closed alveoli. The HFOV gas distribution mechanism ventilates at very fast rates and very small tidal volumes. Figure 1-3 illustrates the HFOV Sensormedic 3100B. When you look at the unit, you will notice that there are no traditional knobs that are most familiar to us as respiratory therapists, yet the principles of ventilation and oxygenation are very clear. If you understand oxygenation as a function of mean airway pressure, and ventilation as a function of amplitude, then you have got it. Unlike conventional ventilation, delivery of the gas happens in both inspiration and expiration. Where we understand exhalation to be passive in our conventional ventilator, it is active in HFOV. Higginson, used the words of Cairo and Pilbeam to describe HFOV:[19]

> Such a system will incorporate an electronic control circuit, or square-wave driver, which powers a linear drive motor. This motor consists of an electrical coil within a magnet, similar to a permanent magnet speaker. When a positive polarity is applied to the square-wave driver, the coil is driven forward. The coil is attached to a rubber bellows, or diaphragm, to create a piston. When the coil moves forward, the piston moves toward the patient airway, creating the inspiratory phase. When the polarity becomes negative, the electrical coil and the attached piston are driven away from the patient, creating an active expiration.

A good way to remember how HFOV works: the more the pistons are displaced that create the oscillations (called amplitude) the bigger the tidal volumes delivered to the patient. Now that we have an understanding of how the oscillator works on the inside, let's discuss each component that simulates ventilator parameters.

Oxygen

1. **Oxygen Blenders**—Most HFOV units are accessorized with oxygen blenders, allowing you to control your fraction of inspired oxygen to the patient.
2. **Mean Airway Pressure**—This knob allows you to adjust the mean airway pressure in order to improve oxygenation. It is recommended to start your mean airway pressure 4 to 5 cm H_2O higher than the MAP of the conventional ventilator settings. Example, if your MAP on conventional ventilation is 25 cm H_2O, then you might start with 29 to 30 cm H_2O to achieve an open lung. It goes without saying that if there is evidence of hemodynamic instability, then it is prudent to reduce the MAP by 2 to 3 cm H_2O, or at least to the MAP on the conventional ventilator settings.
3. **Bias Flow**—As with all ventilators, there must be a knob that adjusts the flow of gas delivered to the patient. The MAP knob is dependent on the bias flow. In fact, you must adjust your bias flow to also adjust your MAP.

Ventilation

1. **Frequency**—This is controlled by your hertz (Hz). One hertz is equal to 60 breaths per minute, and 15 Hz equals 900 breaths per minute (pretty darn fast). Recommended starting Hz is as follows:

Patient	*Weight*	*Hz*
Infant	Under 3 kg	15 Hz
Infant/child	3 kg or greater	10 Hz to 15 Hz
Older child	30 kg or greater	6 Hz to 10 Hz

What you soon recognize is the bigger the child, the less the Hertz, and the more the expected delivered volume of gas.

Remember: A big change in frequency will have a dramatic change on both your amplitude as well as your MAP—think carefully when making a big Hz change.

2. **Power**—This controls chest excursion, which we call "the wiggle factor." A good rule of thumb is to see the wiggle all the way to the belly button: that's a good chest wiggle. If you lose the wiggle, it could mean that you have a displaced the endotracheal tube or there is an obstruction to gas flow. Your ability to hear breath sounds will be replaced with the sound of the piston on the ventilator, so you must adjust your hearing to the sound, the depth, and the pitch of the HFOV. If any of those change, then you can determine that there has been a change in breath sound. Increase the power and you increase the wiggle; decrease the power and you decrease the wiggle.

   Some centers recommend a starting setting of "2." Your PICU may have an established protocol, but if not, start with "2."

   A change in power will affect your MAP, so you will have to readjust your MAP to keep it at the setting that is ordered.
3. **Inspiratory time**—This control is typically set at 33%, which means that 33% of the total time is spent in inspiration:
   33% would give you an I:E ratio of 1:2.
   50% would give you an I:E ratio of 1:1.

When a patient is placed on the oscillator, it is a big deal. Here are some things to consider:

1. The HFOV circuit is an elongated tubing made of highly inflexible material designed not to bend easily. The tubing should remain in a straight line to assure that the frequency of the sound waves has a clear path to the chest wall.
2. When initiating HFOV, make sure that the child is on a hard surface—avoid beds designed to minimize pressure sores because it is difficult to produce oscillation on such a bed.
3. Before starting HFOV, it is strongly recommended to suction the patient thoroughly; breaking the circuit for routine suctioning is discouraged.

The literature supports the use of in-line suction catheters as the standard of care as it minimizes the amount of derecruitment required. **Very Important:** If you must suction, get help. It is better to have two caregivers than just one.

4. Most patients on HFOV will have a properly placed and working arterial line, so monitoring arterial blood gases should never be a problem. If, on the other hand, the arterial line is not available, then noninvasive monitoring with pulse oximetry, and either an end-tidal CO_2 monitor or transcutaneous monitor will work perfectly.

Inhaled Nitric Oxide

In 1987, nitric oxide was found to have some useful benefits in human. Nitric oxide is a colorless, odorless gas that is relatively insoluble in water.[20] Researchers discovered that nitric oxide, once considered a toxic pollutant, had some vasodilation properties on lung tissue.[20] By 1991, researchers were able to prove that inhaled nitric oxide was a selective pulmonary vasodilator in patients with pulmonary hypertension.[20,21,22] Within 2 years, nitric oxide became available to treat patients with acute respiratory distress syndrome; however, its therapeutic use was limited to the pediatric population—or, more precisely, babies with persistent pulmonary hypertension of the newborn (PPHN). At present, inhaled nitric oxide is still the treatment option for PPHN; however, in the case of ARDS, inhaled nitric oxide is used primarily to improve oxygenation for children outside the NICU who do not have PPHN. There have been several studies on the use of nitric oxide in pediatric patients, and the results confirm inhaled nitric oxide's safety and efficacy in treating PPHN;[21,22] however, results from a limited number of studies in the adult population have been inconclusive as to the benefit of nitric oxide for patients with ARDS.

Research shows that inhaled nitric oxide can be given in line with the following mechanical devices: high-frequency jet ventilation (HFJV) with iNO (**Figure 1-4**), conventional ventilation with iNO (**Figure 1-5**), HFOV with iNO in line with circuit (**Figure 1-6**), and HFJV with iNO in line with circuit (**Figure 1-7**). Recently, inhaled nitric oxide has been used

in medical transport for children suffering from PPHN or potential candidates for extracorporeal membrane oxygenation (ECMO). Griffith et al. in their review found animal studies that suggest inhaling nitric oxide at a concentration of 40 ppm for up to 6 months had minimal pulmonary toxicity.[20] Although your PICU/NICU may use its own established protocol, a good starting point for inhaled nitric oxide has been 20 ppm. Because use of inhaled nitric oxide is primarily used for PPHN, similar to what is stated in the literature, iNO has demonstrated immediate results of relaxation to the pulmonary vascular bed for patients other than

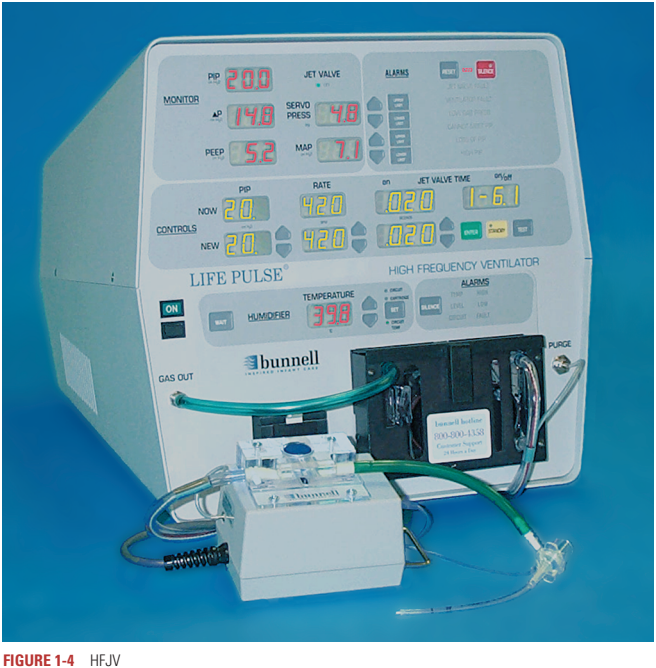

FIGURE 1-4 HFJV

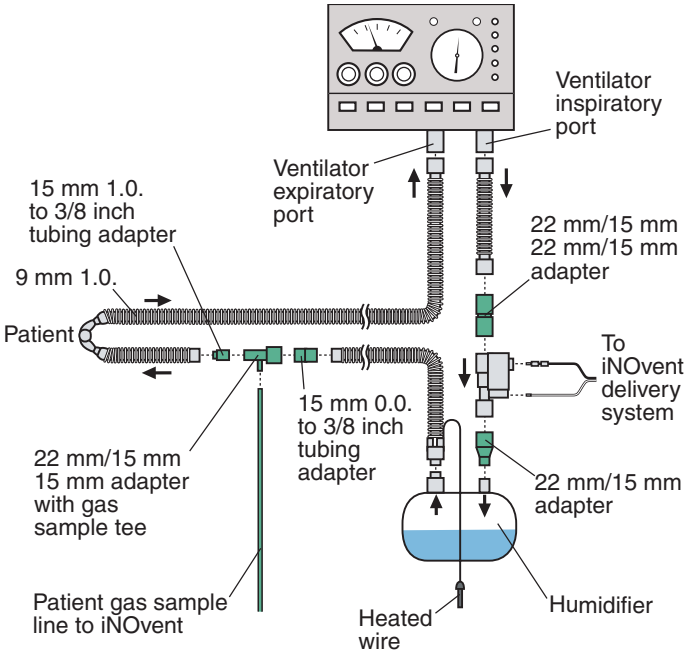

FIGURE 1-5 Conventional ventilator with iNO

PPHN. iNO can be safely used with your conventional adult ventilators, HFOV and HFJV units.

The following are respiratory therapist initial recommendation for iNO:

- Starting setting for iNO: 20 ppm
- Fi02 on the conventional ventilator should be the same for the iNO unit.

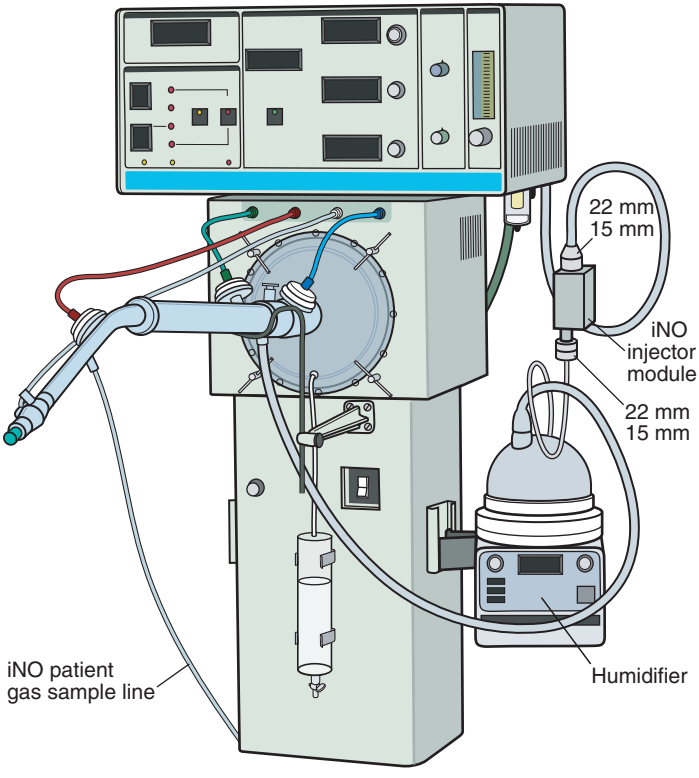

FIGURE 1-6 HFOV with iNO

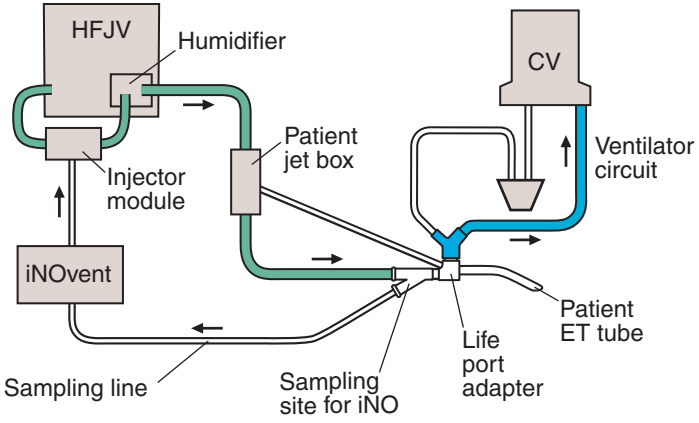

FIGURE 1-7 HFJV with iNO

- Monitor NO_2—keep at less than 3 ppm
- Routinely check patient methemoglobin every 12 to 24 hours depending on your institution

Prone Patient Positioning

Placing the patient on his or her belly to improve oxygenation has been heavily touted in the adult intensive care units for the treatment of ARDS for many years. Our PICU prone positioning experience has been limited; however, prone positioning in the NICU is done routinely. Understanding gas exchange and the implication of ventilation to perfusion mismatch will make this point clear. The lungs have more ventilation to the apices, varying amount of ventilation to the middle of the lungs, and less ventilation to the lower regions where perfusion is greatest. So if you turn the patient on his or her belly, and more specifically head down, the

apices of the lungs will become gravity dependent, which will allow more blood to this area for better perfusion, thus better oxygenation. In 1974, Bryan suggested prone positioning patients on mechanical ventilators; however, his idea was not met with any measurable success. Thirty years later, prone positioning has become one of the treatments for patients with ARDS patients, and, in fact, some medical centers use prone positioning as a routine part of the protocol for ARDS patients.[23,24,25,26] Relvas and colleagues conducted a 3-year retrospective chart review of patients admitted to a pediatric ICU with ARDS and placed in a prone position.[15] Their objectives were to show that placing pediatric patients in the prone position for more than 12 hours would improve their oxygenation index. In fact, those patients who were placed in a prone position for 18 to 24 hours showed the most improvement in their oxygenation index. This group of researchers recommends the use of prone position, provided the patient does not have any contraindications to the prone position.

Relvas and colleagues suggest the following procedures for prone position of a patient:

Preparing the Patient

- Obtain chest x-ray to assure endotracheal tube placement.
- Adequately secure endotracheal tube, pulse oximeter probes, and indwelling catheters.
- Move ECG leads to upper arms and hips.
- Consider capping nonessential vascular catheters and nasogastric tube.
- Suction the oropharynx.
- Apply spongy dressing to pressure point area like knees.
- Assess the need for a special care bed.
- Assign responsibilities to each member of the team responsible for prone positioning of the patient.

Placing the Patient in Prone Position

- Turn the head and body in unison; patient's head should face the ventilator.
- Assess endotracheal tube and indwelling catheters.

- Assess the need to suction.
- Insert pillows or pads under the shoulders and pelvis.
- Flex the arms and position the knees and feet off the bed—use pillow rolls.
- Cushion the forehead.
- Assure that the patient is adequately sedated and pain controlled.
- Assess the need for chest x-ray to reconfirm.
- Slightly reposition every 2 hours.
- Leave the patient in prone position for at least 20 hours.

Contraindication for Prone Position

- Increased intracranial pressure
- Hemodynamic instability despite the administration of vasopressors
- Unstable spinal cord injuries
- Recent abdominal or thoracic surgery
- Open thorax or flail chest
- Inability to tolerate prone position (modified from Relvas et al.[13])

Extracorporeal Membrane Oxygenation

Extracorporeal Membrane Oxygenation (ECMO), most often referred in the literature as extracorporeal life support (see **Figure 1-8**), is a technique developed that is similar to the heart-lung bypass machine used in adults. In children it has been used as a rescue therapy in the early phase of ARDS.[27,28] This therapy is used most often with patients with life-threatening ARDS who have failed other therapies designed to improve oxygenation.

Most of the clinical trials involving pediatric ARDS exclude patients if they have been on conventional ventilation for more than 7 days.[27,28] ECMO has been successfully used in the treatment of infant respiratory distress syndrome for postterm infants diagnosed with PPHN, and the condition is considered reversible. According to Philip Wolfson, the ECMO machine is a modified heart-lung machine that provides for gas exchange in a patient suffering from hypoxemic respiratory failure.[27] ECMO has been used successfully since 1974, treating more than 17,000 infants, with a survival rate of 78%.[18,27,28] During the last few decades,

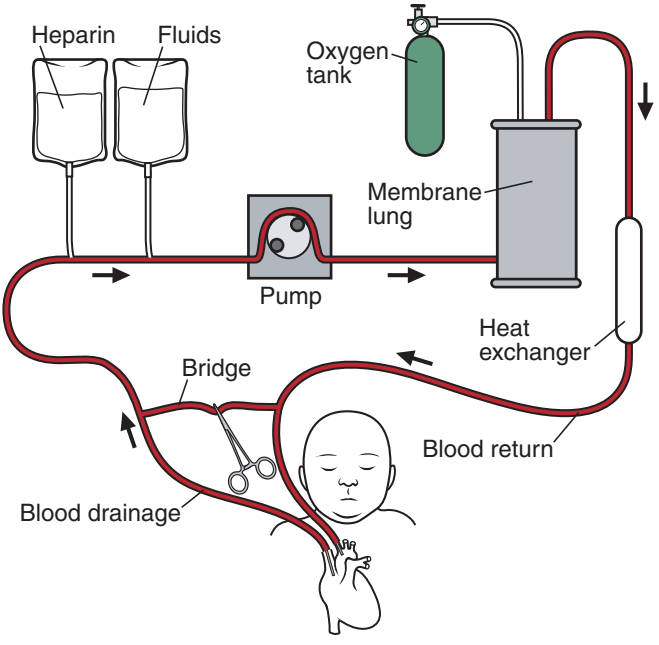

FIGURE 1-8 ECMO diagram

with the introduction of surfactant replacement therapy, inhaled nitric oxide, and better conventional ventilators, ECMO has been reserved for the most severe cases of infants with refractory hypoxemia.

ECMO criteria have been standardized in most ECMO centers. Avery et al. suggest that most ECMO centers base their decisions on one or more of the following established criteria:[28]

TABLE 1-4 Inclusion Criteria for ECMO

ECMO Inclusion Criteria	ECMO Oxygenation Criteria
Gestational age ≥ 34 weeks or birth weight ≥ 2000 grams	$AaDO_2$ 605–620 torr for 4–12 hours
No significant history of bleeding	Oxygen index 35–60 for 0.5–6 hours
No major intracranial hemorrhage	PaO_2 35–50 torr for 2–12 hours
Mechanical ventilation provided less than 14 days	pH less than 7.25 for 2 hours with hypotension
Reversible lung disease	Acute deterioration PaO_2 30–40 torr
No major cardiac lesion	

Heliox Administration

The literature has demonstrated that heliox has shown improvement in oxygenation when used in combination with HFOV for patients with ARDS.[29] Helium is well understood in the treatment of asthma, RSV bronchiolitis, stridor, and other conditions affecting the upper airway.[29] The benefit of helium is due to its low density and the ability to penetrate the narrowed airways. Heliox is commercially available in three mixtures: 70–30, 80–20, and 60–40. The difference between the three mixtures is the density. For example, the density of the 80–20 is 1.178, compared to 60–40, which is 0.678. Heliox has the unique ability to turn turbulent flow into laminar flow; however, in ALI/ARDS, airflow dynamic is less of an issue compared to lung compliance. Current literature supports the use of heliox in combination with other therapies; this is especially true in the treatment of asthma. There is not much research on the use of heliox as a stand-alone therapy in the treatment of ALI/ARDS. **Figures 1-9** and **1-10** will illustrate heliox setup with a nebulizer and with a mechanical ventilator.

Partial Liquid Ventilation

There are several articles that discuss how partial liquid ventilation is used in patients on mechanical ventilation, and the concept seems simple enough, but further review shows that this therapy has not been used often in pediatric patients with ARDS in recent years. Partial liquid ventilation (PLV) is a process that takes the normal lung functional residual capacity and replaces it with perfluorocarbon liquid.[30,31] Perfluorocarbon

FIGURE 1-9 Heliox given with nebulizer

has the ability to dissolve large volumes of oxygen and CO_2 at atmospheric pressure with the ability to reduce surface tension in lungs that are surfactant deficient.[30] The major hurdle of perfluorocarbon is the ability to deliver the liquid to the airway. In this instance, a special ventilation device is needed to move the liquid tidal volume. Thus a modified technique was developed in which you fill the lungs with perfluorocarbon liquid to the functional residual capacity while the remaining gas comes from the conventional ventilator. Much of the research in animal models demonstrated an improvement in oxygenation and carbon dioxide elimination. Leach and her colleagues report that perfluorocarbon worked well in their study because perfluorocarbon was able to reduce surface tension in a diseased lung.[30,31] Leach et al. reported similar findings in

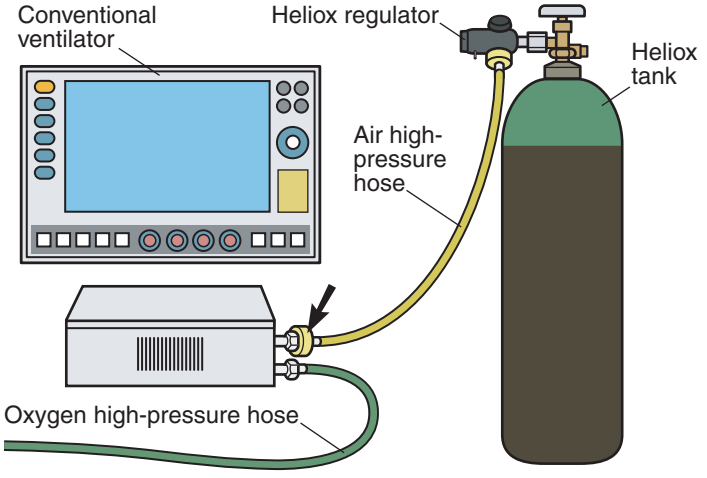

FIGURE 1-10 Heliox in line with mechanical ventilator

their studies with premature infants with respiratory distress syndrome. They showed that within 1 hour after the administration of perflubron (market name for perfluorocarbon), gas exchange improved in the 10 infants in their study.[31] The Cochrane Collaboration conducted a search of the literature on this subject from 1966 to 2003 and found one clinical trial with 182 patients enrolled in the study. This clinical trial was reportedly stopped prematurely and thus was unable to provide convincing results in support of partial liquid ventilation.[32] The Cochrane authors suggest that more robust clinical trials are needed to support the efficacy of partial liquid ventilation in patients with ARDS.

SUMMARY

This chapter provided a reasonable overview of ALI/ARDS regarding the following:

- ✔ What it is—a severe lung injury that can occur because of a number of causes and which results in poor oxygenation despite the high use of oxygen therapy
- ✔ How it presents—some research condenses it into three phases, although Whitaker divides it into four phases:
  - Phase 1: dyspneic, tachypneic, normal oxygenation, normal chest x-ray
  - Phase 2: bilateral infiltrates appear on chest x-ray
  - Phase 3: alveolar-capillary membrane becomes fluid filled in the distal airways and the alveoli, worsening respiratory distress, diffuse infiltrates appear on chest x-ray
  - Phase 4: progressive respiratory failure, lungs become fibrotic, recurrent and resistant pneumonias[6]
- ✔ The importance of PEEP in the treatment of ALI/ARDS
- ✔ How it differs from other conditions like congestive heart failure
- ✔ What the research says about ALI/ARDS
- ✔ And finally, what the available supportive treatment options are

ALI/ARDS is a very complex syndrome that has been well researched, yet its cure is still elusive. Continued research on ALI/ARDS holds promise that one day a cure to this most devastating condition will be available. This author suggests that although research to find a cure is ongoing, the area of supportive care has made significant strides, and as such, respiratory therapists have a number of treatment options that can be recommended for the treatment of ALI/ARDS. This is of particular importance when recommending appropriate modes of ventilation.

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