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Over the past 20 years, there has been increasing attention given to the role of mechanical ventilation in the development of chronic lung disease (CLD) in low birth weight infants. In an attempt to reduce the exposure of the premature lung to the potentially damaging forces (volume and pressure) associated with mechanical ventilation, there has been renewed interest in the role of noninvasive ventilation (NIV) in premature infants.

Noninvasive ventilation is an umbrella term encompassing several types of devices or ventilation strategies. NIV describes devices that provide both continuous positive airway pressure (CPAP) across the respiratory cycle and mechanical "breaths" or phasic increases in airway pressure.¹ Devices that provide CPAP alone are sometimes included in the category of noninvasive ventilation.² Others consider CPAP a separate ventilation strategy.¹ For the purpose of this chapter, CPAP will be included in the discussion of noninvasive ventilation. Where the content is only applicable to CPAP, this is noted.

Types of NIV

CPAP

CPAP is defined as the application of positive pressure to the airways of a spontaneously breathing patient throughout the respiratory cycle. The use of CPAP in adults with respiratory diseases was described as early as the 1930s.³ But it wasn't until the early 1970s that George Gregory, an anesthesiologist working in an NICU, first wrote about its use for neonates with idiopathic respiratory distress syndrome (RDS).⁴ The terms *CPAP* and *PEEP* (positive endexpiratory pressure) are sometimes confused or used interchangeably, but the two mean different things. CPAP is considered a mode of ventilation, while PEEP refers to a level of pressure. During CPAP therapy, the specified amount of pressure is delivered continuously during both the inspiratory and expiratory phases of breathing. During mechanical ventilation, PEEP is generated at the end of exhalation, between delivered breaths and not across the respiratory cycle.

CPAP can be delivered by a variety of devices employing two types of flow: continuous and variable. In the U.S., continuous flow devices are most common and include neonatal ventilators, which provide an ongoing flow of fresh gas while limiting the outflow of gases to deliver the set pressure, and bubble CPAP, which generates pressure when the expiratory tubing is submerged in a chamber of water. The level of water determines the level of pressure generated.

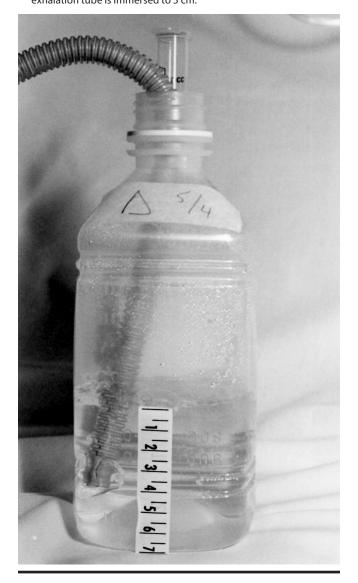
Variable flow devices utilize specialized prongs or masks and flow generators or drivers to maintain the desired airway pressure. With variable flow CPAP, pressure is generated by changing the flow rate of gases during inspiration and expiration to maintain a constant airway pressure or resistance to the flow of gases leaving the nasal prongs or mask.^{5.6}

BUBBLE CPAP

A simple and inexpensive way of generating pressure is to submerge the expiratory tubing in fluid to achieve the desired level of pressure. For example, at Columbia Hospital of New York (CHONY), CPAP is delivered by emptying a one-liter bottle of 0.25 percent acetic acid

FIGURE 8-1 Simple, inexpensive CPAP pressure generation system.

One-liter solution bottle contains 7 cm of 0.25 percent acetic acid; exhalation tube is immersed to 5 cm.



solution to a level of 7 cm and submerging the expiratory end of the CPAP tubing 5 cm into the remaining solution to generate pressure of +5 cm water pressure. The tubing is secured at the neck of the container by a 10 mL syringe with the cap and plunger removed (Figure 8-1). It is not necessary to use acetic acid if it is not available. NICUs that have used sterile water have not reported any problems with overgrowth of bacteria within the outlet bottles.

This simple pressure-generation system is inexpensive, readily available, easily replaced and maintained, as long as heaters and a gas source is available, and does not limit the number of patients who can be on CPAP at any time. Leaving no more than 7 cm of solution in the container eliminates the risk of delivering more than 7 cm of CPAP. Commercial bubble CPAP systems are also available.

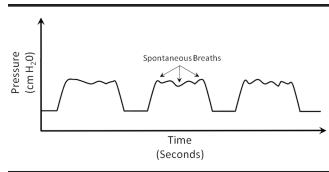
Bubble CPAP produces vibrations similar to highfrequency ventilation. These vibrations have been measured at a frequency of 15–30 Hz.⁷ It has been speculated that the additive effects of these vibrations may account for the positive findings in studies comparing bubble CPAP to ventilator-delivered CPAP.^{8,9} Other researchers have found that the bubbling has no additive effect on oxygenation¹⁰ and that the bubbling effects are dampened by the time the flow reaches the nasal prongs.¹¹

HIGH-FLOW NASAL CANNULA

Nasal cannulae have been used as a method of delivering oxygen to newborns for a number of years. Until recently, the flow rates used with nasal cannulae have been limited by the ability to adequately humidify inspired gases. In the past, higher flow rates resulted in drying and erosion of the nasal tissues. The development of humidification systems has led to increased use of higher flow rates that deliver variable amounts of positive pressure to the infant's lungs. The amount of pressure reaching the infant's lungs will vary according to the type of cannula, the flow rate, and the infant's weight.¹ One study demonstrated that a cannula with an external diameter of 0.3 cm and a flow rate of 2 liters/minute generated a mean pressure of 9 cm H_2O .¹² Another study by Kubicka and colleagues enrolled 27 infants and placed them on high-humidity, high-flow nasal cannula (HFNC) using a catheter with a 0.2 cm outer diameter. They found a linear relationship between flow rate and pressures as long as the infant's mouth was closed. When the mouth was open, no pressure was detected. The highest pressure achieved was $4.5 \text{ cmH}_2\text{O}$ with a flow rate of 8 liters/minute. They concluded that HFNC was not equivalent to CPAP.¹³

Some concern has been raised in using HFNC as a method of delivering positive pressure. Because the nasal cannula has no method of pressure monitoring and no safety release valve, it is essentially delivering unknown levels of pressure.^{1,14} To date, the American Association for Respiratory Care continues to recommend against the use of flow rates greater than 2 liters/minute.¹⁵ Additionally, some studies using HFNC have found increased rates of Gram-negative sepsis.^{16,17} Graham and

FIGURE 8-2 Phasic ventilation.



associates speculate that the increased rate of sepsis may be the result of damage to the nasal mucosa.¹⁶

The system most commonly used, Vapotherm (Vapotherm, Stevensville, Maryland), was recalled in January of 2006 because some infants had developed pneumonia or sepsis caused by Ralstonia, which was traced back to the Vapotherm catheters. The Vapotherm was re-released in January of 2007.⁵ A second device, the HFNC System (Fisher & Paykel RT329, Salter Labs, Arvin, California) is also available in some markets.

NASAL INTERMITTENT POSITIVE PRESSURE VENTILATION (NIPPV)

NIPPV combines with ventilator breaths delivered at a set peak pressure.¹⁸ These increases in airway pressure, can either be delivered at set time intervals (nonsynchronized) known as *nasal intermittent positive pressure ventilation (NIPPV)* or can be triggered by the infant's respiratory efforts (synchronized). Synchronized nasal intermittent positive pressure ventilation (SNIPPV) has been studied more extensively than nonsynchronized NIPPV.

In NIPPV the peak inspiratory pressure, rate, and inspiratory time are all set by the operator.⁶ There are no studies reported that delineate the optimal settings for NIPPV. A review of the topic done by Owen and coworkers notes that rates of 10–25 breaths per minute and PEEP levels of $3-6 \text{ cmH}_2\text{O}$ are the parameters most commonly used in the available research studies.¹⁸

It is unclear by what mechanism NIV confers its proposed benefits to the neonatal lung. For example, it is not known whether breaths are transmitted to the lungs or simply act on the upper airway. In a review of phasic NIV, Moretti and colleagues note that studies have demonstrated variable transmission of breaths with more transmission during synchronous than asynchronous breaths.¹⁹ Other theories explaining the physiologic

Primary Effects of Some Types of NIV
Prevention of atelectasis
Conservation of surfactant
Increased functional residual capacity
Increased airway diameter
Improved diaphragmatic excursion
Decreased intrapulmonary shunting
Decreased respiratory rate and improved respiratory synchrony
Improved lung growth

benefits of phasic NIV include increased pharyngeal dilation, increased respiratory drive, increased tidal volume and minute ventilation, and reduced asynchrony between the chest and abdomen.^{18–22} It is also speculated that SNIPPV may be creating inadvertent PEEP, thereby allowing further recruitment of alveoli, resulting in a higher functional residual capacity (FRC).^{20,23}

NASAL BILEVEL POSITIVE AIRWAY PRESSURE

Bilevel CPAP provides continuous positive pressure at two separate CPAP levels (Figure 8-2). The baseline CPAP level is normally set at $4-6 \text{ cmH}_2\text{O}$, while a second flow meter is set to deliver "sighs" or periods of elevated pressure, usually $2-4 \text{ cmH}_2\text{O}$ higher than the baseline CPAP. A rate is set to determine the frequency of the sighs, and each sigh is usually 0.5-2 seconds long. The Infant Flow SiPAP device (CareFusion, Yorba Linda, California) and the BiPAP system (Respironics, Murrysville, Pennsylvania) are examples of bilevel CPAP devices. As with NIPPV, mechanisms suitable to detect the onset of a neonatal breath are lacking and therefore, at present, no synchronized bilevel CPAP devices are available.

The advantage of bilevel CPAP is thought to come from a higher mean airway pressure and recruitment of unstable alveoli during the sigh breaths. To date, only a few studies have examined SiPAP use in infants. Migliori and colleagues conducted an observational study, which demonstrated that SiPAP provided better gas exchange than conventional CPAP.24 Ancora and associates retrospectively examined the use of SiPAP after surfactant to prevent the need for reintubation. They found that fewer infants in the SiPAP group required mechanical ventilation compared to historical controls.²⁵ Finally, an RCT done by Lista and coworkers compared SiPAP with CPAP for initial support in preterm infants with RDS and found that the infants in the SiPAP group had a shorter duration of mechanical ventilation, shorter length of hospital stay, and less oxygen dependence.²⁶

TABLE 8-2
Comparison of the Effects of Surfactant and CPAP on the Lung and
Alveoli

Characteristic	Effect of Surfactant	Effect of CPAP
Functional residual capacity	Increases	Increases
Alveolar collapse	Prevents at low transpulmonary pressures	Prevents
Intrapulmonary shunting	Decreases	Decreases
Lung compliance	Increases	Increases
Distribution of ventilation	Improves	Improves
Alveolar surface tension	Decreases	Conserves surfactant thereby decreasing surface tension
Surfactant	N/A	Conserves
Transpulmonary pressure	N/A	Increases

NASAL NEURALLY ADJUSTED VENTILATORY ASSIST (NAVA)

NAVA technology has recently been approved by the FDA for both invasive and noninvasive ventilatory support.²⁷ With NAVA, a 5.5 French feeding tube with attached electrodes is positioned in the esophagus at the level of the diaphragm. Nerve impulses in the diaphragm are detected by the electrodes and used to trigger a positive pressure breath. NAVA can be used in small infants and is not affected by the infant's movements or by the air leaks. NAVA devices are currently very expensive and require further research before widespread use.²⁷

BENEFITS OF **NIV**

NIV, including CPAP, has a number of primary effects (Table 8-1). They include preventing atelectasis, conserving surfactant, decreasing intrapulmonary shunting, increasing FRC, increasing compliance, increasing airway diameter and "splinting" the airways and the diaphragm, regularizing respirations and decreasing asynchrony, decreasing respiratory rate, improving lung growth, and mimicking the effects of surfactant. It is important to note that not all NIV devices have been shown to have the same benefits and, in some cases, limited research is available for devices other than CPAP. Much of the work delineating the benefits of CPAP was done during its early use, but more recent studies and reviews of both conventional and bilevel CPAP have confirmed these benefits.^{8,28}

PREVENTION OF ATELECTASIS

Some degree of atelectasis is found in most neonatal respiratory dysfunction, and it results in respiratory distress. For the neonate, the primary benefit of NIV is prevention of atelectasis. NIV provides the pressure necessary to mechanically stabilize the air sacs, preventing their collapse.

Prevention of atelectasis is critical because it is much easier to maintain an expanded alveolus than to reexpand it. CPAP not only prevents alveolar collapse, but also recruits additional alveoli for gas exchange.⁸

CONSERVATION OF SURFACTANT

Surfactant production is low in the premature infant, and available surfactant may be quickly depleted, leading to alveolar collapse. When the alveoli collapse, decreasing the surface area, surfactant is consumed at an even higher rate.⁶ CPAP acts to stabilize the alveolar wall mechanically until production of surfactant is adequate. When used effectively, CPAP mimics the effects of surfactant (Table 8-2).

The early application of NIV is important in decreasing or preventing the loss of existing surfactant. In addition, NIV reduces the chance of damage to Type II pneumocytes that can be caused by the inspiratory pressures generated by mechanical ventilation.

DECREASE IN INTRAPULMONARY SHUNTING

Physiologic shunting within the lung occurs when the web of blood vessels cannot exchange carbon dioxide and oxygen within the collapsed alveolus. When gas exchange does not occur over a widespread area, hypoxia and hypercarbia result. With NIV, shunting of blood decreases, which lessens the ventilation-to-perfusion mismatch and results in improved gas exchange and increased arterial oxygen tension.²⁹

INCREASE IN FUNCTIONAL RESIDUAL CAPACITY

FRC is the air remaining in the lungs after exhalation. It provides an important reserve of air because gas exchange continues between breaths. In many infants with respiratory illness, FRC is greatly diminished, decreasing activity tolerance and increasing the chance of hypoxia. CPAP increases a neonate's ability to adjust to episodes of increased respiratory demand, such as nursing care, medical procedures, feeding, or activity.³⁰

INCREASE IN COMPLIANCE

Improving FRC generally improves compliance as well. NIV keeps the alveoli partially distended, preventing total collapse and making reexpansion during breathing easier. However, lung compliance can decrease if too much distending pressure is applied and the alveoli become overdistended, especially in the presence of a normal lung.³¹

INCREASE IN AIRWAY DIAMETER, AIRWAY AND DIAPHRAGM "SPLINTING"

Through the mechanical action of distending pressure, NIV stabilizes and slightly distends the airways, acting as a splint to keep them open. This increase in airway diameter lowers resistance during both inspiration and exhalation.³⁰ Airway collapse is lessened or prevented, and premature infants exhibit a reduction in obstructive and mixed apnea.^{29,32}

REGULARIZATION OF RESPIRATIONS AND IMPROVED SYNCHRONY

Neonates' breathing patterns become more regular on NIV. Premature infants are prone to periods of irregular breathing and apnea because of their flexible chest structure, immature respiratory drive, and lack of musculature. A neonate on CPAP benefits from the mechanical effects of the distending pressure, which help stabilize the chest wall and reduce thoracic distortion.³⁰ Elgellab and associates demonstrated that CPAP improves thoracoabdominal synchrony and reduces the work of breathing.³³

DECREASE IN RESPIRATORY RATE AND MINUTE VENTILATION

Most newborns on NIV experience a decrease in their respiratory rate, which decreases minute ventilation (minute ventilation = tidal volume × respiratory rate). In spite of the decrease in minute ventilation, the PaCO₂ remains stable or falls, demonstrating that alveolar ventilation is adequate. This likely occurs as a result of an increase in tidal volume and from the recruitment of additional alveoli seen in infants on CPAP.^{33,34}

Improvement in Lung Growth

CPAP has been shown to promote lung growth in animal models. Zhang, Garbutt, and McBride found that use of CPAP with immature animals was associated with increases in lung volume, lung weight, and total lung protein and DNA.³⁵ This strain-induced lung growth may support the practice some NICUs have of using nasal prong CPAP as the primary means of providing respiratory support to infants. These NICUs rarely if ever use nasal cannulas or oxyhoods for ongoing or postextubation care.

DECREASED LUNG INFLAMMATION

Animal studies of bubble CPAP suggest that markers of acute lung inflammation are decreased in preterm lambs compared to lambs receiving mechanical ventilation.³⁶

SECONDARY EFFECTS OF NIV-CPAP

Local changes in cardiac, renal, and cerebral blood flow distribution have been reported as a result of applying distending pressure to the airway. Again, the effects discussed below will vary depending on the device used. These changes, which vary greatly among the studies reporting them, are influenced by the infant's disease process, the NIV delivery system, and the amount of pressure generated.

CARDIAC

The effects of NIV on the infant's cardiac system are directly related to the amount of pressure used. High levels of pressure may impede venous return and have a detrimental effect on cardiac output. In contrast, pressure levels that are appropriate for the newborn's size and lung condition will restore normal intrathoracic pressure and improve overall cardiac function.³⁷

Neonates with hyaline membrane disease often demonstrate right-to-left shunting through the foramen ovale and left-to-right shunting through the ductus arteriosus. This shunting contributes significantly to the hypoxemia, pulmonary fluid retention, and morbidity seen in many newborns with this disease. The effects of distending pressure on cardiac function were studied in premature lambs, and some beneficial effects were found. Shunting through the foramen ovale was decreased, which improved oxygenation. Right ventricular output was increased without significant change in left ventricular output or pulmonary vascular resistance. Left-to-right ductal flow also decreased.³⁸ These physiologic responses to distending pressure improve cardiac output and oxygenation.

Renal

Much of the impact of NIV on the renal system results from changes in cardiac output. If the infant's blood pressure decreases with the application of distending pressure, urinary output, glomerular filtration, and sodium and potassium excretion will be decreased.³⁹ Renal blood flow is either reduced or redistributed. The water- and sodium-retaining hormone systems antidiuretic hormone and aldosterone—are stimulated, producing an antidiuretic effect.^{40,41} These changes are reversed when the distending pressure is withdrawn.

NEUROLOGIC

Some studies suggest that distending pressure increases intracranial pressure.^{42,43} This was especially true in older studies when CPAP is delivered by a head box.^{44,45} In the face of the lower systemic blood pressure seen in infants on distending pressure, there is a drop in cerebral perfusion pressure, which may decrease the risk of intraventricular hemorrhage.⁴² Again, the amount of pressure applied and the infant's lung compliance appear to play important roles in determining the degree of the effect. Higher levels of distending pressure, coupled with less compliant lungs, are associated with higher intracranial pressures and decreased cerebral perfusion pressure.

Comparison of Methods of Providing NIV

Studies comparing various types of NIV have yielded conflicting results. Stefanescu and associates studied 162 extremely low birth weight (ELBW) infants and found no difference in extubation rates between the Infant Flow continuous positive airway pressure system (IF-CPAP) and ventilator-generated CPAP, but infants on variable flow did have fewer days on oxygen and shorter lengths of stay than those on standard CPAP.⁴⁶ Likewise, in a study of 140 infants born between 24 and 29 weeks, Gupta and coworkers also found no difference in extubation failure rates between the group of infants receiving variable flow via the Infant Flow Driver system CPAP, and those receiving bubble CPAP.⁴⁷ Boumecid and colleagues found increased tidal volumes and improved synchrony with the variable-flow CPAP compared to ventilator-generated CPAP in infants with mild respiratory distress.⁴⁸ Liptsen and associates compared bubble CPAP to variable-flow CPAP in 18 infants with birth weights <1,500 g and found that the variableflow CPAP resulted in less asynchrony and less work of breathing than bubble CPAP.⁴⁹ Courtney and coworkers found that lung recruitment was superior with variableflow CPAP than continuous flow. They speculated that this may be a result of the more consistent mean airway pressures seen with variable-flow CPAP.⁵⁰ Finally, in a study of 24 preterm infants, Pandit and colleagues found that infants receiving continuous-flow CPAP had increased work of breathing (13-29 percent higher) over those same infants when they were receiving variableflow CPAP.51

Several studies have been published that compare a high-flow nasal cannula nasal prong CPAP. Sreenan and associates examined the use of HFNC compared to nasal prong CPAP for the management of apnea of prematurity and found that when the HFNC (flow rates of up to 2.5 liters/minute) was used to generate an esophageal pressure of +6 cmH₂O and compared to nasal prong CPAP of $+6 \text{ cmH}_2\text{O}$, there were no differences between the groups in the frequency of apnea.⁵² In a similar study, Saslow and coworkers found no differences in work of breathing in two groups of infants with birth weights of <2 kg, one group receiving NIV via HFNC (3, 4, and 5 liters/minute) and one group receiving NIV via nasal prong CPAP of $+6 \text{ cmH}_2\text{O}$.⁵³ When comparing HFNC to a variable-flow CPAP device, Campbell and colleagues found that infants receiving HFNC had significantly higher rates of reintubation than infants receiving variable-flow nasal prong CPAP.54 However, when Shoemaker and associates compared HFNC to continuous flow CPAP in 101 infants born at 26.5-29.5 weeks gestation, they found a lower rate of extubation failure (18 vs 40 percent) with the early application of HFNC. No differences in the rates of adverse outcomes were noted in this study.¹⁷

In a review of the HFNC studies, Dani and associates concluded that, although some studies have demonstrated benefits of HFNC in preventing reintubation, methodologic issues in these studies render the data inconclusive.⁵⁵ In his review, de Klerk concluded that HFNC should not be regarded as a type of CPAP, but rather as another form of respiratory support.⁵

Several studies have been published that compare either NIPPV or SNIPPV to conventional CPAP. Earlier studies generally used nonsynchronized NIPPV, but more recent studies have focused on NIPPV synchronized (SNIPPV) to the infant's inspiratory efforts. This change requires some degree of caution in interpreting the research data in this area. No studies have compared NIPPV to SNIPPV.¹⁸

Two meta-analyses have been published examining the role of NIPPV in preventing extubation failure and in treating apnea of prematurity.^{56,57} Both of these reviews report on three studies where NIPPV was compared to CPAP after extubation.^{58–60} In each of these studies, NIPPV was found to be superior to CPAP in preventing reintubation. The same meta-analyses evaluated two studies that examined the role of NIPPV in treating apnea of prematurity and found that, though NIPPV may have an advantage over conventional CPAP, the data were not conclusive.^{21,61}

Several studies done since the early 2000s have added support to the efficacy of NIPPV. Using an unblended crossover design, Migliori and coworkers studied 20 infants using two cycles of nasal prong CPAP alternating with NIPPV. These researchers found that during NIPPV, infants had higher transcutaneous oxygen levels (TcPO₂s), lower levels of carbon dioxide, and a decreased respiratory rate.²⁴ A 2007 study of 84 neonates 28-33 weeks of age with RDS done by Kugelman and colleagues found that infants randomized to NIPPV were less likely to require ventilation than the CPAP group (25 vs 49 percent) and were less likely to develop bronchopulmonary dysplasia (BPD) (5 vs 33 percent).⁶² In a randomized study of 63 infants <1,251 g. Moretti and associates compared SNIPPV to nasal prong CPAP after extubation and found that 94 percent of infants on SNIPPV were successfully extubated compared to 61 percent of those receiving nasal prong CPAP.⁶³ Recently, Lista and coworkers compared nasal prong CPAP and bilevel CPAP in infants 28-34 weeks gestational age and found that those on nasal prong CPAP required a longer duration of respiratory support and oxygen therapy and a longer hospital stay than those receiving NIPPV.²⁶

Other studies did not find any difference in tidal volume or minute ventilation when comparing nasal prong CPAP and SNIPPV.^{64,65}

INDICATIONS FOR NIV

There are three primary indications for the use of NIV: (1) respiratory distress of any origin (except congenital diaphragmatic hernia), (2) weaning from mechanical ventilation, and (3) apnea and bradycardia of the premature newborn.

TREATMENT FOR NEONATAL RESPIRATORY DISTRESS

NIV can be very effective in stabilizing the respiratory system while the underlying disease process is evaluated and treated. Common neonatal respiratory problems successfully treated with NIV include RDS, meconium aspiration syndrome, pulmonary edema, transient tachypnea of the newborn (TTN), and BPD. Of these conditions, the use of NIV in the treatment of RDS has received the most attention in the research literature. However, most of the initial studies on CPAP and RDS were done prior to the availability of exogenous surfactant. A meta-analysis of these early studies concluded that the early application of CPAP improved survival in infants <1,500 g.⁶⁶ More recently, attention has been given to the use of NIV in preventing or reducing the severity of BPD. Studies addressing this issue are described below.

The importance of early application of NIV to prevent atelectasis and minimize the downward spiral of acute respiratory distress leading to respiratory failure, must be emphasized. Treatment with NIV is most effective when applied promptly after respiratory distress is recognized. Early application of NIV reduces both the need for intermittent positive pressure ventilation and the duration of respiratory assistance—even in very low birth weight (VLBW) infants.⁶⁶

WEANING FROM MECHANICAL VENTILATION

CPAP has been shown to facilitate weaning from mechanical ventilation and prevent extubation failure. Mechanical ventilation can be harmful even at low settings. The longer an infant is on a mechanical ventilator, the greater the potential for damage to the lungs.⁶⁷ Extubation failures are stressful to the neonate and increase the risk of repeated episodes of atelectasis and reintubation. However, extubation of the relatively stable infant can be considered sooner when oxygen and PEEP can be delivered via NIV.

Espagne and Hascoët showed that when combined with the administration of caffeine, application of nasal prong CPAP resulted in an extubation success rate of 81 percent in their study population of 71 infants, 26.9–31.9 weeks gestational age.⁶⁸ A systematic review looking at the use of CPAP after extubation included nine trials published between 1982 and 2005 and found that CPAP applied immediately after extubation was effective in preventing failure of extubation and adverse events including apnea, respiratory acidosis, and increasing oxygen requirements.⁶⁶

TREATMENT FOR APNEA AND BRADYCARDIA

There are three types of apnea in the neonate: central, obstructive, and mixed. Most neonatal apneas have an obstructive component. Obstructive apnea and mixed apnea are the most responsive to the application of NIV because of its mechanical effect of chest wall stabilization and splinting of the airways and diaphragm. It is thought that CPAP could improve the infant's respiratory drive by stimulating the pulmonary stretch receptors.⁶⁹ Central apnea seems to show little or no response to CPAP.^{70–72} Overall, the evidence supporting CPAP's effectiveness is less clear than that examining extubation failure. A Cochrane review of CPAP for treatment of apnea in neonates found only one trial that met the inclusion

criteria for review and concluded that more study was required. 73

Studies specifically examining NIPPV in the management of apnea of prematurity also showed mixed results. Ryan, Finer, and Peters showed no difference between CPAP and NIPPV in the management of apnea.⁶¹ Lin and colleagues found a more significant reduction in apnea in infants treated with NIPPV than to CPAP.²¹ In a meta-analysis, de Paoli, Davis, and Lemyre found that SNIPPV may be more beneficial than nasal prong CPAP in reducing apnea.⁵⁷ This was confirmed in the Cochrane review comparing NIPPV to nasal prong CPAP for the treatment of apnea of prematurity.⁵⁶

NIV AND BRONCHOPULMONARY DYSPLASIA

BPD results from a complex interaction of factors including incomplete lung development and lung injury and inflammation. Over the years, several definitions of BPD have been used in the literature. In 2000, a consensus conference was held at the National Institutes of Health that resulted in a definition of BPD that included the need for supplemental oxygen for a minimum of 28 days with the amount of oxygen required at 36 weeks postmenstrual age (in infants <32 weeks at birth) determining the severity of disease.⁷⁴ Contributing factors to a diagnosis of BPD include prematurity, mechanical ventilation, barotrauma and volutrauma, pulmonary oxygen toxicity, patent ductus arteriosus, and infection. Intubation with mechanical ventilation has been identified as a major contributing factor to the development of BPD.⁹

Interest in the use of NIV to prevent BPD dates back to the 1980s. In 1987, Avery and associates published a retrospective study in which they compared survival and the incidence of CLD (defined as an oxygen requirement greater than room air at 28 days of age) at eight tertiary neonatal centers. Data were collected between 1982 and 1984 and were adjusted for differences in birth weight, sex, and race. Overall survival rates did not vary significantly among the centers, but the incidence of CLD was much lower at Columbia Presbyterian Medical Center's Babies Hospital (now known as the Children's Hospital of New York at New York Presbyterian Medical Center) than at any of the other seven centers. The main differences in practices between Columbia and the other centers were the early use of nasal prong CPAP, reduced dependence on mechanical ventilation and intubation, permissive hypercapnia (up to 60 mmHg), and the avoidance of muscle relaxants at Columbia.75

In 1994 (nearly ten years later and in the post surfactant era), the International Neonatal Network, in a preliminary analysis of 5,390 infants from 99 hospitals, found that Columbia/CHONY continued to have the lowest adverse event rate, with an adverse event defined as oxygen dependence at 36 weeks postconceptional age, major cerebral damage before discharge, or death.⁷⁶

In 2000, Van Marter and coworkers revisited the issue of variations in respiratory management among NICUs and subsequent differences in the incidence of chronic lung disease (defined as supplemental oxygen at 36 weeks gestational age). The incidence of CLD at Columbia/CHONY was again significantly lower than at the two comparison hospitals (4 percent vs 22 percent).⁷⁷

In 2001, in a historic cohort study, de Klerk and de Klerk documented the results of applying a primarily CPAP-based system of respiratory support, closely modeled on the CHONY system, to a Level III NICU in South Auckland, New Zealand. The study compared the CPAP group with the more conventionally managed historic cohort. The infants ranged in weight from 1,000 to 1,500 g. CLD, defined as the need for supplemental oxygen at 28 days of age, decreased (11 percent in the historic cohort vs 0 percent in the CPAP group). The number of infants requiring mechanical ventilation decreased (65 percent vs 14 percent), as did the number of infants receiving surfactant (40 percent vs 12 percent).⁷⁸ In a follow-up prospective study within the same NICU, continuing the use of the CPAP-based Columbia/CHONY model, Meyer, Mildenhall, and Wong looked at infants weighing <1,000 g and compared their outcomes with those within the Australia and New Zealand Neonatal Network. The investigators noted a reduction in the use of mechanical ventilation, significantly less surfactant use, shorter periods of supplemental oxygen, and a significantly lower requirement for oxygen at 28 days (25 percent vs 63.8 percent) and for oxygen or respiratory support at 36 weeks (19.1 percent vs 45.4 percent).⁷⁹ In a retrospective study, Narendran and colleagues examined the application of bubble CPAP shortly after delivery in 79 infants with birth weights of 401–1,000 g. They found that early CPAP significantly reduced the intubation rate, days on mechanical ventilation, and postnatal steroid use in this population. Although there was a reduction in CLD at 28 days of life, when CLD was defined as any form of respiratory support at 36 weeks gestation there was no difference between the groups.⁸⁰ A recent study evaluating the introduction of bubble CPAP for VLBW infants with RDS found that, with bubble CPAP, fewer infants needed mechanical

ventilation for more than six days (13.6 vs 26.3 percent of historical controls). However, there was no difference in the rate of BPD after the practice change.⁸¹

Given the harmful effects of mechanical ventilation, several studies have investigated whether or not nasal prong CPAP can be used instead of intubation and ventilation in low birth weight infants. Kamper and associates found that using an "early CPAP and permissive hypercapnia" approach when caring for ELBW infants results in lower incidences of chronic lung disease than conventional treatment.⁸² CPAP has been shown to reduce days on ventilation, supplemental oxygen, and BPD.^{78.79,83–90}

While the role of NCPAP in the delivery room is receiving increasing attention, study results have been mixed. In a randomized controlled trial published in 2004, Finer and coworkers found that 80 percent of ELBW infants placed on nasal prong CPAP in the delivery room required mechanical ventilation by one week of age.⁹¹ The CPAP or intubation (COIN) trial was a large multicenter study that set out to determine the role of CPAP in decreasing the rates of BPD and death in preterm infants. Six hundred and ten infants born at 25–28 weeks gestational age were randomly assigned to CPAP (+8 cmH₂O) or intubation and ventilation at five minutes of age. At 36 weeks gestational age, 33.9 percent of the CPAP infants (104) had died or had BPD, compared to 38.9 percent (118) of the intubated group. At 28 days of life, there was a lower risk of death or need for oxygen in the CPAP group (53.7 percent compared to 64.7 percent); 46 percent of the CPAP group required intubation. These investigators concluded that nasal prong CPAP does not reduce the rate of death or BPD in preterm infants.⁹² These findings are similar to those of Sandri and colleagues, who studied the use of CPAP in 230 infants 28-31 weeks gestational age. In this study, CPAP was applied when the infant's FiO₂ reached 40 percent. There was no difference in the need for mechanical ventilation or in long-term outcomes. The CPAP group did have an increased incidence of pneumothorax.93

Surfactant and NIV

Currently, the administration of surfactant requires at least a brief period of mechanical ventilation. Attempts to avoid mechanical ventilation have meant that many of the infants in the previously described studies did not receive surfactant. This may account for the lack of effect shown in some of these studies. Surfactant has been clearly shown to be of benefit to low birth weight infants.94 So many practitioners are moving to an approach first reported in Sweden.⁹⁵ This approach, dubbed INSURE, involves elective intubation, administration of surfactant, and extubation to NIV. The initial study of the INSURE method demonstrated a 50 percent reduction in the number of neonates requiring mechanical ventilation.⁹⁵ Using the same approach, Bhandari and associates found that infants who were intubated, given surfactant, and extubated to SNIPPV had significantly fewer deaths and BPD than infants maintained on conventional ventilation. There were no differences in other morbidities or developmental follow-up scores between the two groups.²³ In a randomized controlled trial of infants 27–32 weeks gestational age assigned to either early CPAP or intubation, surfactant, two minutes of manual ventilation, and extubation, Rojas and associates found that the infants receiving surfactant initially has less need for subsequent intubation and mechanical ventilation (p < .05), fewer air leaks, and less BPD (p < .05) than infants initially placed on CPAP.96

A systematic review examining the use of surfactant combined with extubation to nasal prong CPAP found a decreased need for mechanical ventilation, fewer air leaks, and a decreased rate of BPD in the group receiving early surfactant than in those receiving surfactant later.⁹⁴ Geary and coworkers report on their experience with implementing several practice changes including surfactant with nasal prong CPAP treatment at delivery, lowered oxygen saturation goals, and early amino acid administration. They compared two groups of ELBW infants, one born between 2001 and 2002, and the other born during 2004 and 2005. Implementation of these practice changes resulted in improved morbidity and growth.⁹⁷

On the other hand, Sandri and associates found that INSURE did not offer an advantage over early NCPAP and selective surfactant in decreasing the need for mechanical ventilation or in reducing the incidence of BPD.⁹⁸ A large multi-centered study (SUPPORT trial) examined early NCPAP with intubation and surfactant in ELBW infants and found that BPD rates did not differ between the two groups. There were no differences in the rate of air leaks, necrotizing enterocolitis, intraventricular hemorrhage, or retinopathy of prematurity.⁹⁹ However, this study did not control for the temperature of the gas, level of humidity, and the type and size of nasal prongs that were used. These are important factors to control because cooler, less humidified gases may alter the infant's body temperature and increase cold stress and affect secretions. In addition, some prongs make the work of infant breathing harder. For example, it is a matter of simple physics that longer prongs with a narrow internal diameter will increase resistance and make the work of breathing harder.

A new method for administering surfactant developed by Kribs and colleagues in Germany may eliminate the need for intubation for surfactant and provide further support for the use of NCPAP at delivery. In their study, infants were stabilized on NCPAP and then given surfactant via an intratracheal catheter.¹⁰⁰

Administration of Pressure

Since the use of CPAP began, researchers have been seeking the "optimal" level of PEEP that relieves respiratory distress while causing the fewest complications. At present, no studies have been published that define the optimal levels of distending pressure for NIV. An analysis of data from the 2003 systematic review of nasal prong CPAP trials found no benefit for CPAP levels of <5 cmH₂O;⁶⁶ 5 cmH₂O has been the starting pressure most often recommended in the literature.²⁹

Low levels of PEEP (0–3 cmH₂O) generally do little lung damage and do not cause overinflation, but may not be high enough to overcome atelectasis. In a metaanalysis of CPAP for the prevention of extubation failure, it was found that CPAP <5 cmH₂O was ineffective.⁶⁶ In a study of infants with mild RDS, it was found that infants had the highest end expiratory lung volumes and tidal volumes and the lowest respiratory rates at pressures of 8 cmH₂O.³³ At high levels of PEEP (>8 cmH₂O), complications such as decreased lung compliance, air leak, impaired venous return, and increased PaCO₂ can occur.²⁹

Manipulating the amount of gas flow changes the amount of pressure delivered to the neonate (pressure = flow × resistance). A minimum flow of 5 liters/minute is necessary to generate sufficient pressure and flush carbon dioxide from the system. A maximum flow of 10 liters/minute minimizes the risk of too much distending pressure to the lungs and excessive airflow into the abdomen via the esophagus. Also, flow is a very important component of CPAP because the continuous flow of inspired gas does part of the work of breathing.¹⁰¹

It is important to maintain consistent distending pressure. A loss of pressure forces the infant to increase the work of breathing. That can lead to decreased FRC and compliance and increase symptoms of respiratory distress.

DELIVERING **NIV**

When CPAP was first used in neonates, it was given through an endotracheal tube.⁴ Since that time, a variety of nasal prongs (short, long, single prong, and binasal prongs) and face masks have been developed for neonatal use. There is a dearth of studies comparing various delivery devices.¹⁰²

ENDOTRACHEAL TUBE CPAP

Delivering CPAP by endotracheal tube ensures delivery of a specified amount of pressure directly to the lungs. If the infant deteriorates, mechanical ventilation can begin immediately because the infant is already intubated. However, CPAP delivered by endotracheal tube has some serious drawbacks. The endotracheal tube is longer and narrower than the neonate's trachea. Resistance is increased in tubes with longer lengths and smaller diameters.¹⁰³ CPAP delivered by endotracheal tube is analogous to breathing through a straw. Work of breathing becomes much harder, and fatigue may lead to apnea or symptoms of respiratory distress.

Because endotracheal CPAP is delivered directly to the lungs, it leaves no way for the neonate to "pop off" excess pressure, whether delivered deliberately or inadvertently. The risks of increased levels of PEEP have already been described. Other drawbacks of endotracheal CPAP include laryngeal, tracheal, and vocal cord irritation or damage, increased risk of infection, need for sterile endotracheal suctioning technique, delay of feedings, and undetected endotracheal tube malpositioning.

NASOPHARYNGEAL CPAP

Nasopharyngeal CPAP involves the insertion of one tube or a set of longer prongs through the nares to rest in the pharynx. Although this method avoids the risks associated with endotracheal tubes, it shares the significant problem of increased resistance. To facilitate their passage and decrease trauma, these tubes are narrower than the airway. Because they are also long enough to reach the pharynx, they force the neonate to work harder to breathe.

In addition, these tubes cause moderate to large amounts of secretions. Clearing these secretions to keep the system patent and effective can be difficult and time-consuming. Retropharyngeal abscess secondary to nasopharyngeal CPAP is reported rarely, but remains a potentially serious complication.¹⁰⁴

FACE MASKS

Face masks were once a common method of applying positive pressure. However, with these masks, it was difficult to obtain a seal between the face and the mask that was tight enough to generate positive pressure and yet not damage the skin. During early use, neonatal face mask devices were associated with cerebellar hemorrhage.¹⁰⁵ Additional concerns with face masks include the loss of PEEP during suctioning and reports of gastric distention, especially at high flow rates. Soft silicone masks are now available and provide a better seal without excessive pressure on the face. Currently, there are no published data on the efficacy of these newer masks, and comparisons between face masks and nasal prongs have yet to be reported.¹⁰⁶

In a recent review of nasal prong CPAP, Diblasi notes that, because face masks do not obstruct or narrow the nares, these devices may offer an advantage over binasal prongs. However, this has not yet been tested in research studies.¹⁰⁷ Additionally, face masks can be alternated with nasal prongs to reduce the nasal irritation seen in some infants. Further study is needed to address the use of face masks to provide NIV.

NASAL PRONGS

Nasal prongs are an easy and effective way to deliver NIV. De Paoli and colleagues found that although it remains to be determined which short binasal prongs are the most effective, the evidence suggests that short binasal prongs are more effective in preventing reintubation than are nasopharyngeal tubes.¹⁰⁸ There is limited research comparing the various types of binasal prongs. One study comparing Argyle prongs (Sherwood Medical, St. Louis, Missouri) to Hudson prongs (Hudson RCI, Temecula, California) in premature infants of different birth weights found that both types of prongs were effective in delivering CPAP, but nasal irritation occurred earlier in infants <1,000 g on Argyle prongs. Infants weighing between 1,000 g and 1,500 g in this study had more episodes of prong displacement with the Argyle prongs than the Hudson prongs.¹⁰⁹

Several types of nasal prongs are commercially available for neonates, and each NICU has developed strategies for keeping them in place. Systems that require constant readjustment of nasal prongs, especially for the active infant, have earned NIV the reputation of being hard to work with and not very useful. Careful selection of prong type decreases staff labor and increases NIV effectiveness. The best prongs have the following characteristics:

- They are short, wide, and thin walled, to maximize airflow and decrease resistance.
- They are very soft and flexible, to minimize trauma.
- They are available in a variety of sizes, to ensure a good fit for all neonates.
- They can be easily and firmly secured, even on active neonates, to provide continuous therapy with minimal staff effort.
- Their design minimizes the chance of tissue damage or irritation. Prongs that are set on a bridge do not rest on the face. Prongs that must be set firmly against the nose to generate sufficient pressure may predispose infants to nasal septum breakdown; they should not be used.
- They have tubing that is lightweight and flexible, to allow the infant to be positioned comfortably and the NIV system to be adjusted to him, rather than vice versa.

Nasal prong CPAP has the lowest incidence of pneumothorax of the CPAP delivery types, an incidence that is comparable to that of spontaneous pneumothorax. Another major advantage of nasal prong CPAP is the speed with which the system can be applied and removed. If the equipment is at hand, a trained professional can set up and apply CPAP in only a few minutes, with minimal risk to the infant. The nasal prongs are easy to remove for suctioning and then to replace. The infant's mouth is left free for feedings, pacifiers, or hygiene.

It is also easy to take a stable baby off nasal prong CPAP for a trial. Simply remove the prongs from the nares, and observe the infant for signs of increasing distress. Weaning a chronically ill child from CPAP may be done using an on/off schedule that takes only a few minutes to perform and can be cut short if distress occurs.

Note: Do not discontinue CPAP, even briefly, by shutting off the gas flow and leaving the prongs in place. Because newborns are obligate nose breathers, either the prongs must be removed from the nares or a supply of fresh gas must be provided.

CONTRAINDICATIONS TO NIV

NIV will not benefit all infants requiring respiratory support and in some cases may worsen the infant's condition. At present, the delivery of surfactant requires intubation. Although infants may be intubated, given surfactant, and extubated to NIV, it has been shown that infants with surfactant deficiency who benefit from

FIGURE 8-3

Benign abdominal distention ("CPAP belly") seen in some infants receiving nasal prong CPAP.



From: Jones DB, and Deveau D. 1991. Nasal prong CPAP: A proven method for the reduction of chronic lung disease. *Neonatal Network* 10(4): 7–15. Reprinted by permission.

surfactant should be treated with exogenous surfactant prior to initiating NIV.⁹⁴ However, this study should be considered along with the evidence that was previously discussed; infants who received the Columbia/CHONY nasal-prong CPAP system early (within a minute or two of life) may not have as great a need for surfactant because these infants may have less early-onset atelectasis.

Other contraindications to NIV include congenital anomalies of the airways and lungs and gastrointestinal tract, shock and sepsis, severe apnea, nasal trauma, and the presence of air leak syndromes.^{6,110}

COMPLICATIONS OF NIV

Although less invasive than mechanical ventilation, NIV has a number of possible complications. The incidence and severity of these unintended effects is dependent on the size of the infant, the type of equipment used, the duration of NIV, and the level of distending pressure applied. Reported complications include abdominal distention, feeding disturbances and nasal injury, air leaks, decreased venous return, and decreased cardiac output.^{8,28}

ABDOMINAL DISTENTION

A neonate on nasal prong CPAP may have some gastric and intestinal distention, or "CPAP belly" (Figure 8-3). It is unclear whether the distention is caused by the baby swallowing air, the amount of pressure in the system, decreased gut motility, or a combination of these factors. Research conducted by Jaile-Marti and associates has shown that CPAP belly is benign and can usually be differentiated from distention caused by necrotizing enterocolitis.¹¹¹ The clinical characteristics of a benign CPAP belly are a softly distended abdomen without skin discoloration and stable vital signs. The presence of bowel loops may be a sign of necrotizing enterocolitis or may just be from the CPAP. It is important to recognize that significant abdominal distention will place upward pressure on the diaphragm and may result in respiratory compromise.⁴² One study of NIPPV identified an increased rate of gastrointestinal perforation in the study group.¹¹² But the Cochrane review of NIPPV found no incidence of gastric perforation in the three included studies.^{58–60,113}

Research by Havranek, Madramootoo, and Carver suggests that caution in evaluating infants on nasal prong CPAP is warranted. These researchers studied 18 infants between 21 and 33 weeks gestation, comparing pre- and postprandial intestinal blood flow when the infants were receiving nasal prong CPAP to their blood flow off nasal prong CPAP. They found that both the mean velocity and peak systolic velocity were significantly lower when the infants were on CPAP. The authors postulate that altered intestinal blood flow may impact feeding tolerance.¹¹⁴ Research on bubble CPAP in ELBW infants does not suggest an increased risk of necrotizing enterocolitis following gastric distention caused by CPAP.⁸⁰

NASAL IRRITATION OR SKIN BREAKDOWN

Yong, Chen, and Boo identify nasal septal irritation as a known side effect of NIV.¹¹⁵ A study by Robertson and coworkers found that up to 20 percent of infants in a study of variable-flow CPAP experienced nasal injury. Injuries included necrosis of the columella nasi, flaring of nostrils, and snubbing of the nose.¹¹⁶ Septal injury is usually the result of a combination of friction, pressure, and excessive moisture. It has been speculated that injury to the nasal septum may be the cause of some cases of newborn septicemia.¹¹⁷ The most common cause of nasal trauma is incorrect positioning of the prongs.⁶ Prevention and management of nasal trauma is discussed in the section on nursing care.

AIR LEAKS

Early studies of nasal prong CPAP in preterm infants reported an increased risk of pneumothorax and pneumomediastinum.^{118,119} More recent studies show mixed results. In the COIN trial, infants randomized to early CPAP had a significantly higher incidence of

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pneumothorax (9 percent vs 3 percent).⁹² But a study done by Rojas and colleagues showed a significantly lower risk of air leak in infants receiving CPAP after surfactant and brief ventilation than in those receiving CPAP alone (2 percent vs 9 percent).⁹⁶ The systematic review of six studies in which infants received early surfactant administration and extubation to nasal prong CPAP showed lower rates of air leaks compared to infants given surfactant and continued mechanical ventilation.⁹⁴

CARDIAC COMPROMISE

Cardiac compromise during administration of NIV can occur if pressure levels are high enough to impede venous return.³⁷ A study designed to measure the impact of nasal prong CPAP on cardiac output in preterm infants found decrease in stroke volume or cardiac output when levels of CPAP between 3.5 and 5.3 cmH₂O were used.¹²⁰

CARE OF INFANTS RECEIVING NIV

Caring for an infant receiving NIV poses challenges for care providers. The success of this therapy is largely dependent on keeping the prongs or face mask in the correct position and carefully assessing the infant for the effectiveness of the therapy as well as for the development of complications. Although infants receiving NIV may be less critically ill than some infants receiving mechanical ventilation, appropriate training and nurse:patient ratios remain critical in ensuring patient well-being. All infants receiving NIV should have continuous cardiorespiratory and oxygen saturation monitoring. Blood gases should be evaluated as indicated by the infant's clinical condition.¹²¹

Respiratory Assessment

A system-by-system evaluation of the neonate's response to NIV should be performed regularly to determine the effectiveness of the treatment and to guide care. There are several methods to employ when evaluating an infant's respiratory response and the effectiveness of NIV (Table 8-3). Even in a high-tech hospital environment, skill in physical assessment is important. Many decisions about the management of neonates on NIV are based on observation and physical examination. Infants make many physical adjustments in both method and rate of breathing in an effort to maintain homeostasis *before* technological tools indicate a change in respiratory status.

For example, after a visual assessment of the neonate's retractions, respiratory rate, and overall work of

TABLE 8-3

Evaluation of Respiratory Status

Visual Observation (at rest and when awake)

- Respiratory rate
- Retractions (upper and lower chest)
- Nasal flaring
- Overall work of breathing
- Comparison of upper and lower chest movement (synchronized, lag on inspiration, or seesaw)

Auditory/Auscultation

- Breath sounds
- Grunting (inspiratory or expiratory)

Machine-based Monitoring

- Oximetry
- Blood gas analysis
- Radiography
- Transcutaneous monitoring

breathing, the nurse may conclude that the infant is not breathing comfortably. She may determine that the prongs being used are too small and that air is leaking around them. The decision to change the size of the prongs can be made before any deterioration is evidenced in the infant's oxygen saturation, blood gas values, and/ or x-ray film. All three are often late indications of the degree of respiratory distress.

During a trial off NIV, the infant may become tachypneic and show increased work of breathing by retracting and nasal flaring. The decision to restart the NIV should be based on the neonate's clinical response, even if the oxygen saturation level, blood gas values, and x-ray film remain unchanged. Just as the nurse does not wait for an infant to become hypothermic before initiating interventions to maintain a neutral thermal environment, so must she use physical assessment skills to decide to resume CPAP.

The Silverman-Andersen Retraction Score is available to help quantitate the nurse's visual assessments of the neonate (Chapter 4).¹²² The index can be particularly useful for the nurse who is learning to evaluate respiratory distress. Signs that NIV is effective include a decrease in the infant's work of breathing and improvement in oxygen saturations and blood gases. The infant may remain tachypneic despite a decrease in work of breathing.¹²¹

How frequently the infant's respiratory status should be evaluated depends on the severity of the condition. In most situations, an evaluation every three to four hours is adequate as long as continuous oxygen saturation monitoring is maintained. When evaluating respiratory status, make visual observations of the infant's breathing when at rest and compare these to his breathing when awake or agitated. Visual observations are early indicators of how well the NIV is working, as well as of the severity and progression of the respiratory disease. When the immersion technique for generating pressure is used, the bubbling sounds may interfere with auscultation of breath sounds.

AIRWAY CARE

The percentage of humidity being delivered in the NIV system is an important component of airway care, but one that is often overlooked. As close as possible to 100 percent humidity is optimal. Gas temperatures higher than 36.5°C (97.7°F) have been shown to reduce the severity of CLD and the incidence of pneumothorax.¹²³ One indicator of adequate humidity is the amount of "rain out" in the system. When 100 percent humidity and the gas temperature required to maintain it are being delivered, condensation in the NIV tubing is inevitable. The tubing will need to be emptied every two to three hours or so. If no "rain out" occurs, the percentage of humidity is probably too low.

The critical importance of providing adequate humidity in the system must be emphasized. If the humidity of the gas being administered is not adequate, the infant's mucous membranes become extremely dry, making it difficult to suction the nasopharynx without causing irritation and bleeding. If bleeding occurs, scabs form that may block off part of the airway and cause pain and trauma to the infant whenever suctioning takes place. In addition, without adequate humidity, the infant's secretions will be thicker and more tenacious, making them more difficult to remove and decreasing the effectiveness of the NIV system. Every three hours, the nurse should evaluate and document the temperature of the gas so that appropriate adjustments can be made. High gas temperatures may burn or damage the mucosa of the nasopharynx or lungs. The administration of too cold or too hot gas adversely affects the infant's body temperature. Body temperature outside the neutral thermal range has a negative impact on the infant's respiratory status, including oxygen consumption, blood vessel size, and oxygen saturation. Provision of inadequately humidified gas causes the infant to use energy to warm and humidify the inspired air at the expense of thermoregulation.

When a mouth leak occurs, the unidirectional flow of air through the nose alters the normal humidification process. In a study of adults using nasal prong CPAP for sleep apnea, when participants breathed through their open mouths, nasal resistance and congestion increased considerably. Increasing the amount of humidity relieved congestion and reduced resistance.¹²⁴ According to Poiseuille's law of laminar flow, resistance is inversely proportional to the radius to the fourth power. In other words, if the radius of a tube is halved, resistance is increased 16 times. Thus, an airway blocked by thick secretions, edema, and/or scabs has increased resistance, leading to increased work of breathing and increased signs of respiratory distress. More frequent suctioning is required, but the need for frequent suctioning leads to additional trauma in the area, and a vicious cycle begins.

The airway should be assessed for patency every two to three hours and nares suctioned as necessary.¹²¹ If the infant experiences repeated apnea and bradycardia or shows a gradual decline in oxygen saturation levels, one of the first considerations is to determine whether secretions are blocking the airway. If the infant's nasopharynx is dry and difficult to suction, the use of a few drops of normal saline before suctioning can help lubricate the area and reduce trauma. If the nasal passages are dry or the secretions are extremely thick and tenacious, the humidity of the gas being delivered may need to be reevaluated and increased. It is very important not to suction any more frequently than necessary to avoid creating edema in the nasal passages.

To retrieve secretions that pool in the naso- and oropharynx, it is important to measure suction depth before inserting the catheter. Usually a distance one and one-half times the distance from the pinna to the nares is sufficient. Using a slow, steady insertion, twist, and removal technique is more effective and less traumatic than rapid repeated insertions.

The size of suction catheter needed depends on the size of the infant. If the catheter is too small, suctioning will not be effective, and the infant will have difficulty breathing. If the catheter is too large, it may cause trauma to the area. The larger the catheter, the more effective the yield. Most infants can be suctioned effectively with a #8 French catheter (Figure 8-4).

CARE OF THE NASAL SEPTUM

Meticulous attention to the nasal septum is an important aspect of nursing care for infants on CPAP. There are three main culprits associated with nasal septal breakdown: pressure, friction, and excessive moisture. Increased pressure on the nasal septum decreases circulation in the area, leading to pressure necrosis. Friction causes loss of skin or mucosal integrity.

FIGURE 8-4

A Velcro mustache and nasal suctioning (on room air CPAP).



Use of creams or hydrocolloid barriers in the area of the columella traps moisture, softening the skin and making it more susceptible to injury. They should be used cautiously and only in special circumstances.

Six components are key in helping the nurse maintain the integrity of the infant's nasal septum: (1) the type and size of nasal prongs used, (2) the hat used to anchor and position the tubing and prongs, (3) proper positioning of the neonate and the prongs, (4) use of lightweight tubing, (5) use of a Velcro mustache, and (6) avoidance of creams or routine use of hydrocolloid barriers.

The nurse must frequently assess and document the position of the nasal prongs and the condition of the nasal septum. If an infant begins to show redness of the columella, the nurse must increase the frequency of visual assessments of the area and reassess all six components individually. Occurrence of an injury does not contraindicate the use of CPAP. Prong size and placement can be adjusted to avoid further injury and permit healing while CPAP therapy is continued.

Type and Size of Prongs

The type and size of the nasal prongs used in administering CPAP are the most important component in preventing nasal septum breakdown. Prongs should fit the nares snugly without putting pressure on the nasal septum. Nasal prongs should be large enough to fill the nostrils completely without force, and part of the prong should remain outside the nose (Figure 8-5).¹²⁵ This keeps the bridge of the prongs from pressing into the septum. If the prongs are too small, not only will they allow pressure to escape, compromising the effective delivery of CPAP, but they are also more likely to cause

FIGURE 8-5

Correct size and positioning of nasal prongs for CPAP.

This 18-day-old, 35-week gestation infant remains on CPAP for retractions and tachypnea after extracorporeal membrane oxygenation for congenital diaphragmatic hernia.



From: Jones DB, and Deveau D. 1991. Nasal prong CPAP: A proven method for the reduction of chronic lung disease. *Neonatal Network* 10(4): 7–15. Reprinted by permission.

friction damage as they slide in and out of the nose. Also, the space between the prongs may be too narrow, pinching the septum.

Choosing large prongs that fit snugly helps keep the prongs in place, saving nursing time and decreasing the incidence of nasal irritation; the larger the prongs, the lower the airway resistance. Prong size varies based on the manufacturer's recommendations, the infant's size, and the infant's physical features. For the newborn weighing <700 g, the nostrils may need to be dilated slightly with a cotton swab lubricated in saline to allow a larger prong to fit. Some dilation of the nares occurs during nasal CPAP therapy, but in our clinical experience, the dilation is temporary and diminishes over time, often disappearing before the infant's discharge home.

Hat

A hat that is snug and stationary on the neonate's head serves as an effective anchor for the CPAP delivery system. If the hat moves around, the prongs will move around as well. *Note:* The hats that are provided with commercial prongs do not always fit well or may lose their shape over time and slide off the infant's head. A two- or three-inch- (and occasionally four-inch-) wide stockinette works best. The size of the neonate's head determines the width of the stockinette. Neonates

FIGURE 8-6

Stockinette hat with CPAP tubing secured to the rim.



weighing <1,000 g usually require a two-inch-wide stockinette; those weighing >1,000 g usually need three-inch-wide material.

The length of the stockinette varies as well; 11 inches usually provides enough length to form a two- to threeinch-deep rim and secure the hat at the crown. The rim is made by folding the stockinette twice; the CPAP tubing is secured to the rim (Figure 8-6). A tie or rubber band on the stockinette at the crown of the head helps prevent the hat from slipping down. A more stable double-layered hat may be made by twisting a length of stockinette tubing midway and folding one end back over the other to make a two-layered sack. The open end can then be folded back to make a secure, wide rim.

As the hat loosens with use, the nurse will have more difficulty keeping the CPAP prongs in their proper position. After 24–36 hours, the hat will be stretched out and need to be replaced. Although a snug hat is important, the hat should not be so tight that it leaves ridges in the infant's skin, possibly decreasing perfusion to the area. The wider the brim, the more evenly the pressure of the tubing will be distributed.

Position the hat so that it rests along the lower part of the neonate's ears and across the forehead. Make sure that the infant's earlobes are lying flat, not folded. Clean behind the neonate's earlobes at least daily. If intravenous or arterial lines need to be placed in the FIGURE 8-7

The use of a chest pad to facilitate prone positioning of a 13-dayold infant.



scalp while the infant is on CPAP, a hole may be cut in the hat to facilitate visualization of the site.

Infant Positioning

Labile infants in severe respiratory distress are usually positioned prone or on one side or the other using a small neck roll and supportive nesting rolls and elevating the head of the bed approximately 30 degrees. Keeping the head and neck aligned in the "sniffing" position of mild extension optimizes the airway.¹⁰⁶ Although the prone position is thought to enhance oxygenation, a Cochrane review on positioning for acute respiratory distress found no evidence that the prone position is better than supine or side-lying for nonventilated preterm infants.¹²⁶ Using a pad under the infant's chest is a simple way to position the baby prone (Figure 8-7). Rolls or other creative devices can be employed to facilitate positioning. Swaddling is effective in minimizing movement and can help to prevent tension on the hat or CPAP tubing. An infant on CPAP can easily be placed in a parent's arms or held skin-to-skin; however, overall handling should be limited to decrease the amount of stress on the infant.

Tubing

Lightweight respiratory tubing should be used. In-line water collection bottles should be avoided because the additional weight they add to the tubing can pull the prongs toward the nasal septum. Tubing that twists in one direction or the other makes it more difficult to keep the prongs in the nostrils and the tubing resting lightly on the infant's cheeks. The tubing should be adjusted so that it does not press into the infant's cheeks (see Figure 8-6). Anchor the tubing to the hat using Velcro or safety pins and rubber bands. No matter which method is used, the primary consideration is that the tubing be held securely in place with enough room to make necessary fine adjustments up and down. When using safety pins (see Figure 8-6), point them toward the crown of the infant's head rather than the face. Pass the pins through all thicknesses of the hat rim, being careful not to injure the infant's scalp. Catching all layers of the rim makes a more secure attachment and keeps the hat from being pulled out of shape.

Mustache on the Philtrum

No matter how well the hat fits, how lightweight the tubing is, how the baby is positioned, or the size and type of prongs used, it is difficult in some infants to keep the prongs off the septum. For these infants, a Velcro mustache (see Figure 8-4) placed over a piece of occlusive dressing (such as Tegaderm) or ultrathin hydrocolloid has been used effectively at CHONY and St. Luke's–Roosevelt Hospital Center to maintain the prongs in the proper position. Be sure to size and position the mustache correctly so that the Velcro does not rub against the septum. The moisture in the humidified gas and in nasal and oral secretions will cause the mustache to loosen over time. When that happens, it will need to be removed and replaced so that it does not accidentally dislodge and irritate surrounding tissue or the eyes.

Creams and Barriers

Hydrocolloid barriers are often used under tape to protect the skin of premature infants. However, hydrocolloids do not protect the nasal septum from injury and may actually increase breakdown of the septum by trapping moisture around the nares.⁴³ For mild redness or difficulty in maintaining a seal around the nose, a thin layer of a product such as DuoDERM (Convarec, Skillman, New Jersey) can be used with caution, but should be changed every 12 hours to allow a full assessment of the nares.^{43,127}

PRESSURE DELIVERY MONITORING

The opening and closing of the infant's mouth can cause the amount of pressure being delivered in the system to fluctuate. To maintain consistent pressure delivery, some units apply a chin strap (Figure 8-8). The strap, made from a strip of soft gauze or stockinette, allows the jaw to be pulled gently forward to keep the mouth closed at rest. Even a firm chin strap permits the infant to cry or yawn and allows excess pressure in the circuit to escape if necessary. No increase in aspiration

FIGURE 8-8

A chin strap on a 13-day-old infant born at 27 weeks gestation and 588 g.



of stomach contents has been documented in infants with chin straps. A pacifier can also be used to minimize pressure loss. 125

A sudden loss of all pressure is recognized by lack of bubbling in the solution bottle, an alarm from the pressure monitor, an alarm from the ventilator, a drop in oxygen saturation, or apnea and bradycardia. The loss of pressure may be caused by a leak in the system, such as disconnected tubing, dislocated prongs, or a mechanical malfunction. A system check is warranted to see where the breakdown has occurred. If it is determined that the level of PEEP needs to be adjusted, it is advisable to remove the prongs from the infant's nares before making any changes. Test the system before replacing the prongs. With a bubble CPAP system, vigorous bubbling usually indicates excessive gas flow.

FEEDING

Decisions regarding whether to feed a neonate on NIV are based on his respiratory and physiologic status. There is no contraindication to feeding a stable infant receiving NIV.⁴³ At least one study has shown that gastric emptying time is reduced on CPAP, perhaps because of pressure on the stomach from the diaphragm.¹²⁸

When a neonate is on nasal prong CPAP, tube feeding is given via an orogastric tube. Tube feedings may be given intermittently or maintained as a continuous feeding, depending on the infant's condition. To help reduce the amount of distention, the stomach should be gently aspirated every three to four hours using an orogastric tube and a syringe.⁴³ After aspirating the stomach, remove the tube and document the amount of air obtained. Leaving the orogastric tube indwelling

FIGURE 8-9

Date: Unit: Assessment Performed by:						
Instructions: Record the medical record number of the infant whose CPAP is being	evaluated	ł.				
Mark No for any of the following criteria not met.						
Mark N/A if the criterion is not applicable for this infant at this time.						
Quality Criteria	Medical Record Medical Record No. No.		Record	Medical Record No.		
1. Complete provider order in chart (type of CPAP, flow, pressure, and % O ₂)	🗌 No		🗌 No		🗌 No	
2. Provider order the same as what infant is receiving	🗌 No		🗌 No		🗌 No	
3. CPAP connected to blended air/oxygen gas supply	🗌 No		🗌 No		🗌 No	
4. Flow between 5 and 10 liters/minute	🗌 No		🗌 No		🗌 No	
5. Humidifier temperature and settings set to maintain humidification as close as possible to 100%	🗌 No		🗌 No		🗌 No	
6. Tubing temperature at 37°C (98.6°F)	🗌 No		🗌 No		🗌 No	
7. Humidifier chamber contains water	🗌 No		🗌 No		🗌 No	
8. Neck roll size and position effectively keeping airway in mild extension	🗌 No		🗌 No		🗌 No	
9. Neck roll removed if infant is lying prone	🗌 No	□ N/A	No		🗌 No	
10. Oxygen saturation probe preductal if infant requires more than 21% oxygen	🗌 No	□ N/A	🗌 No	🗌 N/A	🗌 No	🗌 N/A
11. Hat fits snugly with large, wide brim	🗌 No		🗌 No		🗌 No	
12. Nasal prongs fit nares snugly	🗌 No		🗌 No		🗌 No	
13. Nasal prongs not touching the nasal columella (Crossbar between prongs is 2–3 mm clear of columella and septum.)	🗌 No		🗌 No		🗌 No	
14. Nasal prongs not twisted, rotated, or causing lateral septal pressure	🗌 No		🗌 No		🗌 No	
15. Septum intact	🗌 No		🗌 No		🗌 No	
16. Corrugated tubing twisted so it is not touching the infant's face	🗌 No		🗌 No		🗌 No	
17. Corrugated tubing fixed to hat in alignment with prongs	🗌 No		🗌 No		🗌 No	
18. Mustache adhering completely to skin, of appropriate size, clear of eyes, not touching nares or mouth	□ No		🗌 No		🗌 No	
19. Chin strap in place and effectively keeping mouth closed at rest	🗌 No	□ N/A	🗌 No		🗌 No	
20. Head, neck, and body alignment developmentally appropriate	🗌 No		🗌 No		🗌 No	
21. Excess rain out (efferent tubing) drained	🗌 No		🗌 No		🗌 No	
22. Infant receiving 5 cmH ₂ O	🗌 No		🗌 No		🗌 No	
For Bubble CPAP Only:						
a. Tape measure 7 cm mark at base of bottle	🗌 No	□ N/A	🗌 No	🗌 N/A	🗌 No	🗌 N/A
b. Tape measure 0 cm mark at water level	🗌 No	□ N/A	🗌 No	□ N/A	🗌 No	🗌 N/A
c. Tubing securely fixed at 5 cm under water	🗌 No	□ N/A	🗌 No	□ N/A	🗌 No	🗌 N/A
d. Gas bubbling continuously	🗌 No	□ N/A	🗌 No	🗌 N/A	🗌 No	🗌 N/A
23. CPAP system changed according to protocol	🗌 No		🗌 No		🗌 No	
24. Nasal/oral suctioning intervals documented in the nurses' notes every 3 hours during the 24 hours prior to the survey	No	□ N/A	🗌 No	□ N/A	🗌 No	□ N/A
25. Respiratory therapy notes and nurses' notes show no discrepancies during the 24 hours prior to the survey	No		🗌 No		🗌 No	
26. All electrical equipment used in CPAP delivery system has current biomed sticker	🗌 No		🗌 No		🗌 No	

ARC

may lead to unwanted irritation and vagal stimulation without any clinical benefit. An indwelling tube may even increase the amount of air the baby swallows. If the neonate is receiving bolus gavage feedings, aspirate the stomach before feeding him.

Continuous or transpyloric feeding may be of benefit for infants with feeding intolerance.¹ If the neonate is receiving continuous feedings and has some abdominal distention, the feeding may be interrupted and air and stomach contents aspirated gently with a syringe. Any milk aspirated is returned to the stomach, and the continuous feeding is restarted.

Infants on nasal prong CPAP may nipple feed if they are clinically stable. An older, more stable infant who can tolerate short periods off CPAP may be nipple fed without the CPAP, but most infants need CPAP during feeding if they need it at other times. An infant who has passed the acute stage of respiratory illness and is otherwise stable may also be given the opportunity to suckle at the breast. Kangaroo care provides an excellent opportunity for a mother and her premature infant to explore the beginnings of the breastfeeding relationship.

Equipment Maintenance

Changing the Equipment

Because of the high moisture level within an effectively humidified circuit, the NIV equipment should be changed according to the manufacturer's recommendations and unit policy. When changing the equipment of a labile or VLBW infant, it is often necessary for two people to work together. All of the new equipment should be connected and checked to be sure that it is functioning before the old system is removed. Infants weighing <1,000 g are often dependent on NIV and may experience apnea and bradycardia immediately when taken off the system. These usually resolve quickly when the NIV is replaced.

Troubleshooting

Frequent apnea and bradycardia or a decrease in oxygenation in the infant on NIV requires an examination of the equipment to look for any leaks in the system. The baby is checked for hyper- or hypoflexion of the neck, which could cause narrowing of the trachea. If no external mechanical problem is identified, the neonate should be suctioned gently and quickly to check for blockage of the airway by secretions. The most common blockage location is in the nasopharynx.

Depending on the equipment being used, excessive bubbling, an increase in pressure, or increased

TABLE 8-4

Indications for Mechanical Ventilation in Neonates at CHONY

- Marked retractions on CPAP
- Frequent, prolonged apnea on CPAP
- $PaO_2 < 50 \text{ mmHg with } FiO_2 0.8-1.0$
- PaCO₂ >65 mmHg (after stabilization)
- Cardiovascular collapse
- Unrepaired congenital diaphragmatic hernia

Adapted, courtesy of Columbia Presbyterian Medical Center, New York.

abdominal distention can be caused by excessive flow rates. The range of flow for all babies is between 5 and 10 liters/minute. Most infants require a flow of 6-8 liters/minute. If the flow is set too low, carbon dioxide may be retained in the system.

STAFF COMPETENCY VALIDATION AND QUALITY IMPROVEMENT

Competency validation of staff caring for infants on NIV helps ensure the delivery of high-quality, consistent care. Regular quality improvement surveys should be done to document that the standard of care is being met and to identify any deficiencies. Figure 8-9 depicts one data collection tool that can be used for this purpose. *Note:* This tool can be easily modified to document validation of clinical competence in caring for infants on a variety of NIV devices.

Each case of nasal septal erosion should be reported, evaluated, and analyzed. These data are useful in determining if there is a need for improvement strategies within the unit and among the clinical staff. Some of the variables reviewed are staffing patterns, nursing assignments, staff competency review, introduction of new products into the unit, and evaluation and scrutiny of the entire NIV setup. Multiple factors affect the incidence of nasal septal damage, making it an excellent routine multidisciplinary quality improvement surveillance activity.

CPAP FAILURE CRITERIA

Although CPAP may be used successfully by an experienced staff on even very ill, labile infants, there are limitations to its application. Determining when an infant receiving NIV needs intubation and mechanical ventilation is dependent on a number of factors. It is important for the clinician to consider the infant's gestational age, weight, and underlying medical condition. No specific parameters have been determined by research, but De Paoli and associates suggest the following as indications for intubation: significant episodes of apnea, a PCO₂ exceeding 60 mmHg, and the need for more than 60 percent oxygen to achieve acceptable oxygen saturations.¹⁴ The risk:benefit ratio of any decision involving an invasive procedure must be carefully considered. Table 8-4 outlines the criteria for mechanical ventilation used at CHONY.

WEANING FROM CPAP

There are no evidence-based guidelines that identify the optimal approach to weaning infants from NIV. The postdelivery age at which infants are ready to be weaned from NIV can vary greatly. For example, a term infant with TTN may require CPAP for only a few hours, but an infant weighing <1,000 g may remain on room-air CPAP for several weeks because of apnea, bradycardia, and a high potential for atelectasis. The need for supplemental oxygen in the absence of cyanotic heart disease is a sign of lingering respiratory disease. Generally, weaning is initiated when the work of breathing normalizes, oxygen requirements are minimal, and the infant is not having significant apneic and bradycardic episodes. Another sign that the infant may be ready to be weaned from NIV is tolerance of short periods off of support, such as during weighing or position changes, without an increase in work of breathing or oxygen requirements.

When phasic NIV has been used, the backup rate is normally decreased, and then the infant is switched to CPAP. The CPAP pressures are then gradually weaned until they reach 4 or 5 cmH₂O. Depending on the etiology of the respiratory distress, infants may be weaned from CPAP to nasal cannula.

During a trial off CPAP, careful attention needs to be paid to maintaining a clear airway, supporting thermoregulation, and reducing energy expenditure during the trial. The initial trial-off period may last for from one to several hours. There may be some initial tachypnea as the infant adjusts to the loss of pressure support. But if this period passes without apnea, bradycardia, decreased in oxygen saturation, or other signs of worsening distress, then the trial is considered successful. Any infant taken off NIV who does not breathe comfortably and at a regular rate, or who has frequent apnea and bradycardia is not ready to be weaned from NIV.

SUMMARY

Noninvasive ventilation is a safe, effective, and relatively inexpensive method of providing ventilatory support to infants in mild to moderate respiratory distress. Early application of NIV is especially beneficial to treat symptoms and to prevent further deterioration. There is growing evidence supporting the use of NIV as a strategy to decrease the incidence and severity of BPD in low birth weight infants.

It is important to recognize that not all NIV devices have been shown to have the same benefits and, in some cases, limited research is available for devices other than CPAP. Regardless of the NIV delivery system used, careful patient assessment, attention to detail, and evidence-based practice grounded in known physiologic principles remain important nursing responsibilities. The successful use of NIV is dependent on the appropriate selection and application of equipment and on vigilant monitoring of the infant.

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References

- 1. Courtney SE, and Barrington KJ. 2007. Continuous positive airway pressure and noninvasive ventilation. *Clinics in Perinatology* 34(1): 73–92.
- 2. Soll RF. 2007. A review on noninvasive ventilation: The Cochrane Systematic Reviews 2006. *Journal of Perinatology* 27(Supplement 1): S21–S25.
- Barach AL. 1936. The therapeutic use of helium. *JAMA* 107(16): 1273–1280.
 Gregory GA, et al. 1973. Treatment of idiopathic respiratory distress
- syndrome with continuous positive airway pressure. New England Journal of Medicine 284(24): 1333–1340.
- 5. de Klerk A. 2008. Humidified high-flow nasal cannula: Is it the new and improved CPAP? *Advances in Neonatal Care* 8(2): 98–106.
- 6. Davis PG, Morley CJ, and Owen LS. 2009. Non-invasive respiratory support of preterm neonates with respiratory distress: Continuous positive airway pressure and nasal intermittent positive pressure ventilation. *Seminars in fetal and Neonatal Medicine* 14(1): 14–20.
- Lee KS, et al. 1998. A comparison of underwater bubble continuous positive airway pressure with ventilator-derived continuous positive airway pressure in premature neonates ready for extubation. *Biology of the Neonate* 73(2): 69–75.
- Donn SM, and Sinha SK. 2003. Invasive and noninvasive neonatal mechanical ventilation. *Respiratory Care* 48(4): 426–439.
- 9. Ramanathan R, and Sardesai S. 2008. Lung protective ventilatory strategies in very low birth weight infants. *Journal of Perinatology* 28(Supplement 1): S41–S46.
- 10. Morley CJ, et al. 2005. Nasal continuous positive airway pressure: Does bubbling improve gas exchange? *Archives of Disease in Childhood. Fetal and Neonatal Edition* 90(4): F343–F344.
- 11. Kahn DJ, et al. 2007. Unpredictability of delivered bubble nasal continuous positive airway pressure: Role of bias flow magnitude and nares-prong air leaks. *Pediatric Research* 62(3): 343–347.

- 12. Locke RG, et al. 1993. Inadvertent administration of positive end-distending pressure during nasal cannula flow. *Pediatrics* 91(1): 135–138.
- 13. Kubicka ZJ, Limauro J, and Darnall RA. 2008. Heated, humidified high-flow nasal cannula therapy: Yet another way to deliver continuous positive airway pressure? *Pediatrics* 121(1): 82–88.
- 14. De Paoli AG, Morley C, and Davis PG. 2003. Nasal CPAP for neonates: What do we know in 2003? Archives of Disease in Childhood. Fetal and Neonatal Edition 88(3): F168–F172.
- American Association for Respiratory Care. 2002. Selection of an oxygen delivery device for neonatal and pediatric patients—2002 revision and update. Retrieved January 4, 2010, from http://www.rcjournal.com/cpgs/ pdf/06.02.707.pdf.
- 16. Graham PL III, et al. 2006. Risk factors for late onset Gram-negative sepsis in low birth weight infants hospitalized in the neonatal intensive care unit. *The Pediatric Infectious Disease Journal* 25(2): 113–117.
- Shoemaker MT, et al. 2007. High flow nasal cannula versus nasal CPAP for neonatal respiratory disease: a retrospective study. *Journal of Perinatology* 27(2): 85–91.
- Owen LS, Morley CJ, and Davis PG. 2007. Neonatal nasal intermittent positive pressure ventilation: What do we know in 2007? Archives of Disease in Childhood. Fetal and Neonatal Edition 92(5): F414–F418.
- 19. Moretti C, et al. 1999. Comparing the effects of nasal synchronized intermittent positive pressure ventilation (nSIPPV) and nasal continuous positive airway pressure (NCPAP) after extubation in very low birth weight infants. *Early Human Development* 56(2-3): 167–177.
- 20. Khalaf MN, et al. 2001. A prospective randomized, controlled trial comparing synchronized nasal intermittent positive pressure ventilation versus nasal continuous positive airway pressure as modes of extubation. *Pediatrics* 108(1): 13–17.
- Lin CH, et al. 1998. Efficacy of nasal intermittent positive pressure ventilation in treating apnea of prematurity. *Pediatric Pulmonology* 26(5): 349–353.
- 22. Kiciman NM, et al. 1998. Thoracoabdominal motion in newborns during ventilation delivered by endotracheal tube or nasal prongs. *Pediatric Pulmonology* 25(3): 175–181.
- Bhandari V, et al. 2007. A randomized controlled trial of synchronized nasal intermittent positive pressure ventilation in RDS. *Journal of Perinatology* 27(11): 697–703.
- Migliori C, et al. 2005. Nasal bilevel vs. continuous positive airway pressure in preterm infants. *Pediatric Pulmonology* 40(5): 426–430.
- 25. Ancora G, et al. 2010. Role of bilevel positive airway pressure in the management of preterm newborns who have received surfactant. *Acta Paediatrica* 99(12): 1807–1811.
- 26. Lista G, et al. 2010. Nasal continuous positive airway pressure (CPAP) vs bi-level nasal CPAP in preterm babies with respiratory distress syndrome: A randomized control trial. Archives of Disease in Childhood. Fetal and Neonatal Edition 95(2): F85–F89.
- DiBlasi RM. 2011. Neonatal noninvasive ventilation techniques: Do we really need to intubate? *Respiratory Care* 56(9): 1273–1294.
- Polin RA, and Sahni R. 2002. Newer experience with CPAP. Seminars in Neonatology 7(5): 379–389.
- 29. Davis PG, and Morley CJ. 2008. Noninvasive respiratory support: An alternative to mechanical ventilation in preterm infants. In *The Newborn Lung*, Bancalari E, ed. Philadelphia: Saunders, 361–376.
- Locke R, et al. 1991. Effect of nasal CPAP on thoracoabdominal motion in neonates with respiratory insufficiency. *Pediatric Pulmonology* 11(3): 259–264.
- Bancalari E, and del Moral T. 2006. Continuous positive airway pressure: Early, late, or stay with synchronized intermittent mandatory ventilation? *Journal of Perinatology* 26(supplement 1): S33–S37.
- 32. Miller MJ, et al. 1990. Effects of nasal CPAP on supraglottic and total pulmonary resistance in preterm infants. *Journal of Applied Physiology* 68(1): 141–146.
- 33. Elgellab A, et al. 2001. Effects of nasal continuous positive airway pressure (NCPAP) on breathing pattern in spontaneously breathing premature newborn infants. *Intensive Care Medicine* 27(11): 1782–1787.
- 34. Durand M, McCann E, and Brady JP. 1983. Effect of continuous positive airway pressure on the ventilatory response to CO2 in preterm infants. *Pediatrics* 71(4): 634–638.
- Zhang S, Garbutt V, and McBride JT. 1996. Strain-induced growth of the immature lung. *Journal of Applied Physiology* 81(4): 1471–1476.
- Jobe AH, et al. 2002. Decreased indicators of lung injury with continuous positive expiratory pressure in preterm lambs. *Pediatric Research* 52(3): 387–392.
- Sherman TI, et al. 2003. Physiologic effects of CPAP: Application and monitoring. Neonatal Network 22(6): 7–16.

- Cotton RB, et al. 1980. Effect of positive-end-expiratory-pressure on right ventricular output in lambs with hyaline membrane disease. *Acta Paediatrica Scandinavica* 69(5): 603–606.
- Fewell JE, and Norton JB Jr. 1980. Continuous positive airway pressure impairs renal function in newborn goats. *Pediatric Research* 14(10): 1132–1134.
- 40. Annat G, et al. 1983. Effect of PEEP ventilation on renal function, plasma renin, aldosterone, neurophysins and urinary ADH, and prostaglandins. *Anesthesiology* 58(2): 136–141.
- Hall SV, Johnson EE, and Hedley-Whyte J. 1974. Renal hemodynamics and function with continuous positive-pressure ventilation in dogs. *Anesthesiology* 41(5): 452–461.
- Upadhyay A, and Deorari AK. 2004. Continuous positive airway pressure—a gentler approach to ventilation. *Indian Pediatrics* 41(5): 459–469.
- Bonner KM, and Mainous RO. 2008. The nursing care of the infant receiving bubble CPAP therapy. Advances in Neonatal Care 8(2): 78–95.
- 44. Gabriele G, et al. 1977. Continuous airway pressure breathing with the headbox in the newborn lamb: Effects on regional blood flows. *Pediatrics* 59(6): 858–864.
- Aidinis SJ, Lafferty J, and Shapiro HM. 1976. Intracranial responses to PEEP. Anesthesiology 45(3): 275–286.
- 46. Stefanescu BM, et al. 2003. A randomized, controlled trial comparing two different continuous positive airway pressure systems for the successful extubation of extremely low birth weight infants. *Pediatrics* 112(5): 1031–1038.
- 47. Gupta S, et al. 2009. A randomized controlled trial of post-extubation bubble continuous positive airway pressure versus Infant Flow Driver continuous positive airway pressure in preterm infants with respiratory distress syndrome. *Journal of Pediatrics* 154(5): 645–650.
- Boumecid H, et al. 2007. Influence of three nasal continuous positive airway pressure devices on breathing pattern in preterm infants. Archives of Disease in Childhood. Fetal and Neonatal Edition 92(4): F298–F300.
- Liptsen E. et al. 2005. Work of breathing during nasal continuous positive airway pressure in preterm infants: A comparison of bubble vs variable-flow devices. *Journal of Perinatology* 25(7): 453–458.
- Courtney SE, et al. 2001. Lung recruitment and breathing pattern during variable versus continuous flow nasal continuous positive airway pressure in premature infants: An evaluation of three devices. *Pediatrics* 107(2): 304–308.
- Pandit PB, et al. 2001. Work of breathing during constant- and variable-flow nasal continuous positive airway pressure in preterm neonates. *Pediatrics* 108(3): 682–685.
- 52. Sreenan C, et al. 2001. High-flow nasal cannulae in the management of apnea of prematurity: A comparison with conventional nasal continuous positive airway pressure. *Pediatrics* 107(5): 1081–1083.
- Saslow JG, et al. 2006. Work of breathing using high-flow nasal cannula in preterm infants. *Journal of Perinatology* 26(8): 476–480.
- Campbell DM, et al. 2006. Nasal continuous positive airway pressure from high flow cannula versus infant flow for preterm infants. *Journal of Perinatology* 26(9): 546–549.
- 55. Dani C, et al. 2009. High flow nasal cannula therapy as respiratory support in the preterm infant. *Pediatric Pulmonology* 44(7): 629–634.
- 56. Lemyre B, Davis PG, and de Paoli AG. 2002. Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for apnea of prematurity. *Cochrane Database of Systematic Reviews* (1): CD002272.
- 57. De Paoli AG, Davis PG, and Lemyre B. 2003. Nasal continuous positive airway pressure versus nasal intermittent positive pressure ventilation for preterm neonates: A systematic review and meta-analysis. *Acta Paediatrica* 92(1): 70–75.
- Barrington KJ, Bull D, and Finer NN. 2001. Randomized trial of nasal synchronized intermittent mandatory ventilation compared with continuous positive airway pressure after extubation of very low birth weight infants. *Pediatrics* 107(4): 638–641.
- 59. Friedlich P, et al. 1999. A randomized trial of nasopharyngeal-synchronised intermittent mandatory ventilation versus nasopharyngeal continuous positive airway pressure in very low birth weight infants after extubation. *Journal of Perinatology* 19 (6 part 1): 413–418.
- 60. Khalaf MN, et al. 1999. A prospective randomized, controlled trial comparing synchronized nasal intermittent positive pressure ventilation (SNIPPV) versus nasal continuous positive airway pressure (NCPAP) as mode of extubation. *Pediatric Research* 45: 204A.

- Ryan CA, Finer NN, and Peters KL. 1989. Nasal intermittent positive-pressure ventilation offers no advantages over nasal continuous positive airway pressure in apnea of prematurity. *American Journal of Diseases of Children* 143(10): 1196–1198.
- 62. Kugelman A, et al. 2007. Nasal intermittent mandatory ventilation versus nasal continuous positive airway pressure for respiratory distress syndrome: A randomized, controlled, prospective study. *Journal of Pediatrics* 150(5): 521–526.
- 63. Moretti C, et al. 2008. Nasal flow-synchronized intermittent positive pressure ventilation to facilitate weaning in very low-birthweight infants: Unmasked randomized controlled trial. *Pediatrics International* 50(1): 85–91.
- 64. Aghai ZH, et al. 2006. Synchronized nasal intermittent positive pressure ventilation (SNIPPV) decreases work of breathing (WOB) in premature infants with respiratory distress syndrome (RDS) compared to nasal continuous positive airway pressure (NCPAP). *Pediatric Pulmonology* 41(9): 875–881.
- 65. Ali N, et al. 2007. Effects of non-invasive pressure support ventilation (NI-PSV) on ventilation and respiratory effort in very low birth weight infants. *Pediatric Pulmonology* 42(8): 704–710.
- 66. Ho JJ, et al. 2002. Continuous distending pressure for respiratory distress syndrome in preterm infants. *Cochrane Database of Systematic Reviews* (2): CD002271.
- 67. Gau GS, Ryder TA, and Mobberley MA. 1987. Iatrogenic epithelial change caused by endotracheal intubation of neonates. *Early Human Development* 15(4): 221–229.
- Espagne S, and Hascoët JM. 2002. Noninvasive ventilation of premature infants. Archives de Pédiatrie 9(10): 1100–1103.
- 69. Speidel BD, and Dunn PM. 1976. Use of nasal continuous positive airway pressure to treat severe recurrent apnoea in very preterm infants. *Lancet* 2(7987): 658–660.
- Martin RJ, et al. 1977. The effect of low continuous positive airway pressure on the reflex control of respiration in the preterm infant. *Journal of Pediatrics* 90(6): 976–981.
- Miller MJ, Carlo WA, and Martin RJ. 1985. Continuous positive airway pressure selectively reduces obstructive apnea in preterm infants. *Journal of Pediatrics* 106(1): 91–94.
- Kattwinkel J, et al. 1975. Apnea of prematurity. Comparative therapeutic effects of cutaneous stimulation and nasal continuous positive airway pressure. *Journal of Pediatrics* 86(4): 588–592.
- 73. Henderson-Smart DJ, Subramaniam P, and Davis PG. 2001. Continuous positive airway pressure versus theophylline for apnea in preterm infants. *Cochrane Database of Systematic Reviews* (4): CD001072.
- 74. Jobe AH, and Bancalari E. 2001. Bronchopulmonary dysplasia. American Journal of Respiratory Critical Care Medicine 163(7): 1723–1729.
- 75. Avery ME, et al. 1987. Is chronic lung disease in low birth weight infants preventable? A survey of eight centers. *Pediatrics* 79(1): 26–30.
- 76. Tarnow-Mordi W. 1994. International comparisons of hospital performance. International Neonatal Network Newsletter No. 4.
- Van Marter LJ, et al. 2000. Do clinical markers of barotrauma and oxygen toxicity explain interhospital variation in rates of chronic lung disease? *Pediatrics* 105(6): 1194–1201.
- 78. de Klerk AM, and de Klerk R. 2001. Nasal continuous positive airway pressure and outcomes in preterm infants. *Journal of Paediatrics and Child Health* 37(2): 161–167.
- 79. Meyer M, Mildenhall L, and Wong M. 2004. Outcomes for infants weighing less than 1000 grams cared for with a nasal continuous positive airway pressure-based strategy. *Journal of Paediatrics and Child Health* 40(1-2): 38–41.
- Narendran V, et al. 2003. Early bubble CPAP and outcomes in ELBW preterm infants. *Journal of Perinatology* 23(3): 195–199.
- Nowadzky T, Pantoja A, and Britton JR. 2009. Bubble continuous positive airway pressure, a potentially better practice, reduces the use of mechanical ventilation among very low birth weight infants with respiratory distress syndrome. *Pediatrics* 123(6): 1534–1540.
- Kamper J, et al. 1993. Early treatment with nasal continuous positive airway pressure in very-low-birth-weight infants. Acta Paediatrica 82(2): 193–197.
- Jacobsen T, et al. 1993. "Minitouch" treatment of very-low-birth-weight infants. Acta Paediatrica 82(11): 934–938.
- 84. Gittermann MK, et al. 1997. Early nasal continuous positive airway pressure treatment reduces the need for intubation in very low birth weight infants. *European Journal of Pediatrics* 156(5): 384–388.
- Lindner W, et al. 1999. Delivery room management of extremely low birth weight infants: Spontaneous breathing or intubation? *Pediatrics* 103(5 Part 1): 961–967.

- 86. Joris N, Sudre P, and Moessinger A. 2000. Early application of CPAP in newborns with gestational age below 34 weeks lowers intubation rate and shortens oxygen therapy without altering mortality and morbidity. *Schweizerische Medizinische Wochenschrift* 130(49): 1887–1893.
- 87. Aly H, et al. 2004. Does the experience with the use of nasal continuous positive airway pressure improve over time in extremely low birth weight infants? *Pediatrics* 114(3): 697–702.
- Miksch RM, et al. 2008. Outcome of very low birthweight infants after introducing a new standard regime with the early use of nasal CPAP. *European Journal of Pediatrics* 167(8): 909–916.
- 89. Kirchner L, et al. 2005. Is the use of early nasal CPAP associated with lower rates of chronic lung disease and retinopathy of prematurity? Nine years of experience with the Vermont Oxford Neonatal Network. *Journal of Perinatal Medicine* 33(1): 60–66.
- 90. te Pas AB, and Walther FJ. 2007. A randomized, controlled trial of deliveryroom respiratory management in very preterm infants. *Pediatrics* 120(2): 322–329. (Published erratum in *Pediatrics*, 2007, 120[4]: 936.)
- Finer NN, et al. 2004. Delivery room continuous positive airway pressure/ positive end-expiratory pressure in extremely low birth weight infants: A feasibility trial. *Pediatrics* 114(3): 651–657.
- 92. Morley CJ, et al. 2008. Nasal CPAP or intubation at birth for very preterm infants. *New England Journal of Medicine* 358(7): 700–708. (Published erratum in *New England Journal of Medicine*, 2008, 358[14]: 1529.)
- Sandri F, et al. 2004. Prophylactic nasal continuous positive airways pressure in newborns of 28–31 weeks gestation: Multicentre randomised controlled clinical trial. Archives of Disease in Childhood. Fetal and Neonatal Edition 89(5): F394–F398.
- 94. Stevens TP, et al. 2007. Early surfactant administration with brief ventilation vs. selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome. *Cochrane Database of Systematic Reviews* (4): CD003063.
- 95. Bohlin K, et al. 2007. Implementation of surfactant treatment during continuous positive airway pressure. *Journal of Perinatology* 27(7): 422–427.
- 96. Rojas MA, et al. 2009. Very early surfactant without mandatory ventilation in premature infants treated with early continuous positive airway pressure: A randomized, controlled trial. *Pediatrics* 123(1): 137–142.
- 97. Geary CA, et al. 2008. Improved growth and decreased morbidities in <1000 g neonates after early management changes. *Journal of Perinatology* 28(5): 347–353.
- Sandri F, et al. 2010. Prophylactic or early selective surfactant combined with NCPAP in very preterm infants. *Pediatrics* 125(6): e1402–e1409.
- 99. Finer NN, et al., 2010. SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Early CPAP versus surfactant in extremely preterm infants. New England Journal of Medicine 362(21): 1970–1979.
- 100. Kribs A, et al. 2010. Surfactant without intubation in preterm infants with respiratory distress: First multi-center data. *Klinische Padiatrie* 222(1): 13–17.
- 101. Katz JA, Kraemer RW, and Gjerde GE. 1985. Inspiratory work and airway pressure with continuous positive airway pressure delivery systems. *Chest* 88(4): 519–526.
- 102. Wisewell TE, and Srinivasan P. 2003. Continuous airway pressure. In Assisted Ventilation of the Neonate, 4th ed., Goldsmith JP, and Karotkin EH, eds. Philadelphia: Saunders, 127–147.
- 103. Wall MA. 1980. Infant endotracheal tube resistance: Effects of changing length, diameter, and gas density. *Critical Care Medicine* 8(1): 38–40.
- 104. Jones SW, and King JM. 1993. Retropharyngeal abscess secondary to nasopharyngeal CPAP in a preterm neonate (letter). Archives of Disease in Childhood 68(5 Special No.): 620.
- 105. Pape KE, Armstrong DL, and Fitzhardinge PM. 1976. Central nervous system pathology associated with mask ventilation in the very low birthweight infant: a new etiology for intracerebellar hemorrhages. *Pediatrics* 58(4): 473–483.
- 106. Morley C, and Davis P. 2004. Continuous positive airway pressure: Current controversies. *Current Opinion in Pediatrics* 16(2): 141–145.
- Diblasi RM. 2009. Nasal continuous positive airway pressure (CPAP) for the respiratory care of the newborn infant. *Respiratory Care* 54(9): 1209–1235.
- 108. De Paoli AG, et al. 2008. Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates. *Cochrane Database of Systematic Reviews* (1): CD002977.
- 109. Rego MA, and Martinez FE. 2002. Comparison of two nasal prongs for application of continuous positive airway pressure in neonates. *Pediatric Critical Care Medicine* 3(3): 239–243.

- 110. Hutchison AA, and Bignall S. 2008. Non-invasive positive pressure ventilation in the preterm neonate: Reducing endotrauma and the incidence of bronchopulmonary dysplasia. Archives of Disease in Childhood. Fetal and Neonatal Edition 93(1): F64–F68.
- 111. Jaile-Marti J, et al. 1992. Benign gaseous distension of the bowel in premature infants treated with nasal continuous airway pressure: A study of contributing factors. *American Journal of Roentgenology* 158(1): 125–127.
- 112. Garland JS, et al. 1985. Increased risk of gastrointestinal perforations in neonates mechanically ventilated with either face mask or nasal prongs. *Pediatrics* 76(3): 406–410.
- 113. Davis PG, Lemyre B, and de Paoli AG. 2001. Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation. *Cochrane Database of Systematic Reviews* (3): CD003212.
- 114. Havranek T, Madramootoo C, and Carver JD. 2007. Nasal continuous positive airway pressure affects pre- and postprandial intestinal blood flow velocity in preterm infants. *Journal of Perinatology* 27(11): 704–708.
- 115. Yong SC, Chen SJ, and Boo NY. 2005. Incidence of nasal trauma associated with nasal prong versus nasal mask during continuous positive airway pressure treatment in very low birthweight infants: A randomised control study. Archives of Disease in Childhood. Fetal and Neonatal Edition 90(6): F480–F483.
- Robertson NJ, et al. 1996. Nasal deformities resulting from flow driver continuous positive airway pressure. Archives of Disease in Childhood. Fetal and Neonatal Edition 75(3): F209–F212.
- 117. Ronnestad A, et al. 2005. Septicemia in the first week of life in a Norwegian national cohort of extremely premature infants. *Pediatrics* 115(3): e262–e268.
- Hall RT, and Rhodes PG. 1975. Pneumothorax and pneumomediastinum in infants with idiopathic respiratory distress syndrome receiving continuous positive airway pressure. *Pediatrics* 55(4): 493–496.

- Ogata ES, et al. 1976. Pneumothorax in the respiratory distress syndrome: incidence and effect on vital signs, blood gases, and pH. *Pediatrics* 58(2): 177–183.
- 120. Moritz B, et al. 2008. Nasal continuous positive airway pressure (n-CPAP) does not change cardiac output in preterm infants. *American Journal of Perinatology* 25(2): 105–109.
- Askin DF. 2007. Noninvasive ventilation in the neonate. Journal of Perinatal & Neonatal Nursing 21(4): 349–358.
- 122. Silverman WA, and Andersen DH. 1956. A controlled clinical trial of effects of water mist on obstructive respiratory signs, death rate and necropsy findings among premature infants. *Pediatrics* 17(1): 1–10.
- 123. Tarnow-Mordi WO, et al. 1989. Low inspired gas temperature and respiratory complications in very low birth weight infants. *Journal of Pediatrics* 114(3): 438–442.
- 124. Richards GN, et al. 1996. Mouth leak with nasal continuous positive airway pressure increases nasal airway resistance. *American Journal of Respiratory Critical Care Medicine* 154(1): 182–186.
- Bohlin K, et al. 2008. Continuous positive airway pressure and surfactant. Neonatology 93(4): 309–315.
- 126. Wells DA, Gillies D, and Fitzgerald DA. 2005. Positioning for acute respiratory distress in hospitalized infants and children. *Cochrane Database of Systematic Reviews* (2): CD003645.
- 127. McCoskey L. 2008. Nursing Care Guidelines for prevention of nasal breakdown in neonates receiving nasal CPAP. *Advances in Neonatal Care* 8(2): 116–124.
- 128. Gounaris A, et al. 2004. Gastric emptying in very-low-birth-weight infants treated with nasal continuous positive airway pressure. *Journal of Pediatrics* 145(4): 508–510.

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