Infant Respiratory Distress Syndrome (IRDS)

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CHAPTER 2

CHAPTER OUTLINE

DEFINE

Prematurity
• Define infant respiratory distress syndrome (IRDS)
Postmaturity
• Define transient tachypnea of the newborn (TTN)
• Define meconium aspiration syndrome (MAS)
• Define congenital diaphragmatic hernia (CDH)
• Define persistent pulmonary hypertension of the newborn (PPHN)
• Define surfactant replacement therapy (SRT)

RESEARCH

• Relevant research on IRDS
• Relevant research on surfactant replacement therapy (SRT)

TREATMENT

• Treatment options in the care of IRDS patients
• Respiratory therapist role in the management of IRDS

DISTINGUISH

• Neonatal pneumonia with group B streptococcus (GBS)
• Neuromuscular disease
• Mechanical restrictive problems

KEY TERMS

Acute lung injury
Acute respiratory distress syndrome
Extracorporeal membrane oxygenation (ECMO)
High-frequency oscillatory ventilation (HFOV)
Infant respiratory distress syndrome
Inhaled nitric oxide
Lung protective strategy
Mechanical ventilator
INTRODUCTION

When first asked by the author to write a chapter in this book, I was elated; it was the highest compliment that anyone could afford me. I thought, finally I can put to paper my various experiences as a neonatal pediatric specialist in respiratory care. I can recall some hair-raising stories that really challenged me and brought every bit of my respiratory knowledge, experience, and education into play. I could not wait to have a venue to share these experiences, and hopefully help other healthcare professionals avoid some of the pitfalls and embarrassing moments that, through trial and error, I have had to endure.

As an experienced respiratory therapist in a neonatal intensive care unit, I have seen the hope and hopelessness of many parents who were told that their child had one of the manifestations of infant respiratory distress syndrome (IRDS). The prognosis for these infants can be dismal and depends on so many influences before, during, and after the delivery. There is always hope, and as the compassionate clinician, you find yourself hoping right along with the parents. Although modern medicine has improved the mortality and morbidity of these children, there are many treatment procedural possibilities that you, the bedside clinician, might recommend. These treatment options can bring about a positive change.

This chapter will focus on the most prominent life-threatening entities that result in IRDS: prematurity of the newborn, transient tachypnea of the newborn (TTN), congenital diaphragmatic hernia (CDH), meconium aspiration syndrome (MAS), and persistent pulmonary hypertension of the newborn (PPHN). Research has shown that preterm and term infants are more likely to suffer from any one of these conditions soon after birth. The key to successful management for these babies is early recognition and early action.

DEFINE

By definition, the word *syndrome* means a certain set of established signs and symptoms occurring concurrently to indicate a disease process to an organ or system. The National Institutes of Health and the U.S. National Library of Medicine define infant respiratory distress syndrome
Infant Respiratory Distress Syndrome (IRDS) as a complication that can make it difficult for the premature infant to breathe. Infant respiratory distress syndrome that is called hyaline membrane disease (HMD) or respiratory distress syndrome (RDS) is a condition that affects the terminal bronchioles and alveolar ducts in which the hyaline membrane is a fibrinous material composed of blood and cellular debris. The lining of the lungs are ruddy in appearance and airless, and the main feature of this condition is widespread diffuse atelectasis. IRDS is caused by the absence of proper surfactant production due to an immature or poorly developed lung, such as that seen in the premature infant. In the postmature lungs, IRDS is the result of disruption of airflow with subsequent atelectasis causing an acute lung injury. Other causes of IRDS can be categorized as genetic deficiencies that affect lung development, lung structural defects, diaphragmatic abnormalities, phrenic nerve abnormalities, and/or rib cage defects. The main cause of IRDS is a lack of surfactant, which prohibits the lungs from expanding and recoiling. The inability of the lungs to expand creates a ventilation perfusion mismatch or shunt, which leads to poor oxygenation of the blood, or hypoxemia. The lack of perfusion to the poorly developed lungs prevents circulation of oxygen to vital organs. Although IRDS is seen predominantly in the premature infant, the respiratory therapist is often asked to see infants who display signs and symptoms of respiratory distress several hours after birth. Consider the following conditions.

Transient tachypnea of the newborn is the increase in respiratory rate, greater than 60, of a newly born infant. Historically, it was believed that TTN happened most often in babies born through cesarean section, but this belief is still controversial. Avery et al. conclude that TTN is the delayed reabsorption of lung fluid at the time of birth. It is believed that TTN is the result of an immature surfactant system, which showed a lack of phosphatidylglycerol in amniotic fluid. Risk factors include prematurity, maternal sedation, maternal bronchodilator therapy for asthma during pregnancy, maternal increase in fluids during pregnancy, and fetal asphyxia.

Meconium aspiration syndrome occurs when the fetus passes fecal material that has accumulated during gestation (usually due to fetal stress) into the amniotic fluid and the fecal material is aspirated into
the fetus’s lungs. Interestingly, the term *meconium* comes from the Greek word *mekoni*, meaning poppy juice or opium. Meconium-stained infants admitted to the nursery tend to reflect an infant who is under the influence of the same drugs that the mother has received. The word *mekoni* refers to the subdued response shown by these infants, similar to how one would act under the influence of opium. Meconium is a viscous green liquid material composed of gastrointestinal secretions, cellular debris, bile and pancreatic juice, mucus, blood, lanugo, and vernix. Meconium aspiration contributes to fetal asphyxiation and very low venous PaO₂ prior to birth of the infant. Fetal asphyxiation occurs as a result of the infant’s gasping respiratory efforts that allow meconium into the respiratory tract. Meconium that is detected below the vocal cords is indicative of meconium aspiration syndrome.

Congenital diaphragmatic hernia is a hole in the wall of the diaphragm that permits abdominal content to migrate into the chest cavity. This migration results in poorly developed lungs, a heart that has shifted, and profound cyanosis and respiratory distress at birth.

Persistent pulmonary hypertension of the newborn, formally known as persistent fetal circulation (PFC), is the persistent elevation of pulmonary vascular pressure in a newborn in the absence of any other recognizable conditions. Avery and colleagues refer to this condition as the “failure to make the transition from high pulmonary vascular resistance (PVR) and low pulmonary blood flow, characteristic of the fetus, to the relatively low PVR and high pulmonary blood flow of the postnatal infant.”

**Clinical Note**

A newborn’s grunt, the sound produced when breathing against a closed glottis, is the equivalent of the amazing concept of PEEP (positive end-expiratory pressure). Observation reveals that at the end of each inspiration, an infant grunts. The infant will actually hold his or her breath for a second, bear down, and grunt just before exhalation. The infant may be observed using accessory muscles, tachypneic, and nasal flaring. This simple maneuver builds pressure in the lungs, forcing oxygen across the alveolar capillary membrane. It also helps to maintain patency of the alveolar sacs. Although grunting is somewhat effective at keeping the patient’s oxygen level up, the infant’s work of breathing is also increased, which makes it less likely that the infant is able to continue this effort for very long.
Depending on the effort the infant is exerting, the respiratory therapist may be asked to provide supplemental oxygen and/or pressure to the patient who is grunting to relieve some of the work of breathing. This can be provided via nasal CPAP or the more recent and friendlier method of a high humidity nasal cannula. The infant is watched carefully for signs of tiring. At the first sign of the infant becoming tired, usually a decrease in oxygen saturation as displayed on a pulse oximeter, it may become necessary to utilize additional interventions. It is extremely important for the clinician to keep a careful eye on this type of patient. There should be frequent monitoring of the respiratory rate and the patient's oxygen saturation. If the patient deteriorates, intervention has to happen quickly.

**Describe**

Infant respiratory distress syndrome, or hyaline membrane disease (HMD), is described in low or extremely low birth-weight babies who present with respiratory distress within the first minutes to hours following birth. This condition manifests itself when there is a lack of surfactant production in the lungs. The infant’s lungs become lined with damaged lung cells and protein, which leaks into the alveoli-capillary bed, causing the alveoli to be lined with hyaline cartilage. Hyaline membranes form in response to the damaged lung. These membranes make it difficult for the lung to expand and, more important, for oxygen to cross the alveolar capillary membrane into the bloodstream, which prevents vital organs from being oxygenated. The following are some of the symptoms of infants with respiratory distress:

- Cyanosis
- Apnea
- Decreased urine output
- Nasal flaring
- Puffy or swollen arms or legs
- Rapid breathing
- Shallow breathing
- Shortness of breath and grunting sounds while breathing
- Paradoxical chest wall movement with breathing
- Increased oxygen requirement
Breath sounds that include rales
- Poor lung aeration
- Accessory muscle usage
- Chest x-ray showing atelectasis, air bronchograms, and granular infiltrates

The clinical course of an infant with respiratory distress syndrome depends on the size and maturity of the infant. The more profound clinical symptoms appear in the extremely low birthweight and early gestational age babies: those who weigh less than 1000 grams and are born at gestational age of less than 25 weeks.

Transient tachypnea of the newborn is described as a sudden increase in respiratory rate shortly after birth that usually continues for 2 to 5 days. Symptoms of TTN include grunting and retractions. This condition is self-limiting and usually subsides within a few days. If the infant displays moderate to severe symptoms of distress, consideration must be given to maintaining adequate oxygenation and ventilation.

Meconium aspiration syndrome occurs in about 10%–15% of all births. The infant’s skin may be stained with the yellowish-green meconium, his or her nail beds may have the meconium caked under them and be blue, and often you can visualize meconium in the oropharynx. The infant’s respiratory efforts are directed toward getting oxygen to the lungs and tissue. Aspiration of meconium causes a mechanical obstruction in the lungs, further preventing effective oxygenation. Avery et al. indicated that MAS produces decreased lung tissue compliance and parenchymal lung damage.

Additionally, MAS produce a ball-valve mechanism that partially closes the airway and contributes significantly to air trapping, increased expiratory lung resistance, and increased functional residual capacities. In complete closure of the airway, the result of widespread atelectasis and significant perfusion ventilation mismatch will occur. In babies with severe MAS, this leads to pulmonary hypertension with right-to-left shunting. The following are typical signs of MAS:

- Tachypneic
- Nasal flaring
Retractions
• Cyanosis

Congenital diaphragmatic hernia usually involves profound cyanosis with severe respiratory distress at birth. There is urgency in this infant to reverse the hypoxia, hypercarbia, and metabolic acidosis that is evident at birth. Historically, this was an operative condition that required immediate surgery; however, this condition now requires aggressive pre-surgery treatment to manage oxygenation and ventilation to avoid the devastation associated with persistent pulmonary hypertension of the newborn. Poor oxygenation is secondary to poorly oxygenated blood being shunted through the foramen ovale and the ductus arteriosus causing a right-to-left shunt. Failure to reverse these sequences of events could result in the infant’s death.

Persistent pulmonary hypertension of the newborn is the delay of the fetal circulation to transition from the prebirth systemic circulation to the postbirth systemic circulation. Avery et al. describes the transition in four phases:

• In utero phase—immediate phase that occurs in the first minutes after birth and is characterized as PVR that exceeds systemic vascular resistance. In utero blood bypasses the lung.
• Immediate phase—fluid-filled fetal lungs are distended with the first breath. PVR is decreased with the rapid entry of air into the alveoli.
• Fast phase—accounts for the greatest reduction in PVR, which occurs 12 to 24 hours after birth. A drop in PVR has been associated with an increase in the production of prostacyclin and nitric oxide, which are vasodilators.
• Final phase—results in the remodeling of the pulmonary vascular musculature. In a normal fetal and term lung, fully muscularized, thick-walled preacinar arteries extend to the level of the terminal bronchioles. Hypoxia at birth prevents this remodeling of smooth muscle.

PPHN usually affects full-term babies who are born with a continuation of hypoxemia despite the lack of significant lung disease. Typical signs of respiratory distress are indistinguishable from many other conditions
that affect infants; however, a careful maternal history often reveals signs of perinatal asphyxia. PPHN must be distinguished so that appropriate treatment is implemented. Causes of PPHN, such as MAS, IRDS, and congenital diaphragmatic hernia, are discussed elsewhere in this chapter.

**NICU Respiratory Therapist Factoids**

I recall an extremely busy shift, and at the end of my shift I did not have time to replace the equipment I had used during the shift. I relayed this situation in report, and the oncoming therapist was appalled. I was reminded that failure to replace equipment used was unacceptable. This seemingly innocent oversight could cost time and energy to find and set up equipment, which ultimately would hinder the ability to provide the necessary clinical expertise that would be needed at that very moment. At first glance, I was offended; however, as I thought more about the situation, I realized that the oncoming respiratory therapist was right. NICU and pediatric intensive care units (PICU) tend to be fast paced, and because of time limitations, the urgency with which the patient needs intervention, there is an expectation that different types of equipment be set up and ready to go. Nowhere is this more important than in a NICU or PICU. If this means that the person on the off-going shift needs to stay a little longer to set things up and restock supplies, then so be it. When called upon to set up equipment to manage a very unstable patient with PPHN, there are no moments for hesitation. In the future, you and your colleagues will learn to appreciate this more than you will ever know. In reality, this is just a level of respect and professionalism that every clinician should have.

**DISTINGUISH**

There are several conditions that mimic IRDS at birth. The three most common conditions are neonatal pneumonia with group B streptococcus (GBS), neuromuscular diseases, and mechanical restrictive disorders. There are many more conditions that would easily fit into this category; however, this chapter will highlight the above mentioned, because they are more likely to be seen in a NICU or PICU setting.

Neonatal pneumonia with group B streptococcus (GBS) occurs quite often in the neonate. It can be acquired transplacentally, during the birth process, or postnally. GBS is the most common bacteria that affect neonate in the first week of life, occurring from 1.3 to 3 per 1000 live births. GBS is found in the genital and intestinal flora of pregnant women, and the bacteria are easily able to pass from mother to baby. A chest x-ray is
helpful in distinguishing GBS from infant respiratory distress syndrome. It may show pleural effusion, increased vascular markings, or patchy infiltrates.\textsuperscript{6}

Werdnig-Hoffman disease, also known as infantile spinal muscular atrophy type I, is a degenerative neuromuscular disease of the spinal motor plate (see Chapter 10 for a full discussion). Often this is detected in utero: the mother notices that there has been a cessation of movement in an otherwise active fetus. At birth, the infant will show signs of
respiratory distress with profound weakness, retractions, and abdominal
distention.3

Myasthenia gravis can occur in newborn, although it is thought to
be rare. Faranoff and Martin discuss two forms: (1) neonatal myasthenia
gravis, which occurs only in mothers with myasthenia gravis, and (2)
congenital myasthenia gravis, which occurs in mothers without a his-
tory of myasthenia gravis. In both forms of myasthenia gravis, the infant
displays respiratory difficulty immediately after birth, with signs of gen-
eralized weakness, feeble cry, poor sucking, facial weakness, and ptosis.3
Maternal history is the key to distinguishing this form of infant respira-
tory distress.

There are a number of neonatal upper airway obstructions that often
present immediately after birth and cause significant respiratory distress.
Of these mechanical restrictive problems, choanal atresia, Pierre Robin
syndrome, and tracheoesophageal fistula are the more common airway
obstructions observed in the NICU.

Choanal atresia is a malformation of the nasopharynx area. New-
borns are considered obligate nose breathers and must learn to breathe
through their mouth immediately. Signs of cyanosis are present at birth.
Establishment of an airway is required followed by corrective surgery.

Pierre Robin syndrome is a combination of undersized jaw, cleft of
the soft palate, and a tongue that falls toward the back of the throat,
causing airway obstruction. Infants with this condition have respiratory
difficulty, with cyanosis, poor feeding, and failure to thrive.

Tracheoesophageal fistula is a communication between the stomach
and the esophagus that may lead to aspiration pneumonia. Children with
this condition produce copious amounts of secretions that lead to chok-
ing. Careful monitoring of these infants is necessary because in severe
circumstances respiratory distress may progress to respiratory failure.

**RESEARCH**

Advances in medical management of infant respiratory distress syndrome
have changed the natural course of this condition. Improvement in antenatal
corticosteroid administration to mothers at risk for premature delivery,
surfactant replacement therapy, and much more sophisticated
conventional ventilator used in the delivery room play a role in reducing the incidence of IRDS. Geoffrey Argons et al. reported in 2002 that the number of infants born before 37 weeks’ gestation in the United States was 487,000, which represented 12.1% of all live births and a 14% increase from 1990. Their report attributes this rise in preterm birth to the increase number of multiple births secondary to fertility therapy. Medical management of the preterm infant has improved significantly, resulting in the management of preterm infants as young as 23–24 weeks’ gestational age. Historically, infants this young would not survive extrauterine life, due to their pulmonary immaturity, which leads to severe tissue damage and poor gas exchange. The introduction of surfactant replacement therapy has dramatically improved the mortality of these infants and subsequently has lowered morbidity. Instillation of surfactant in the preterm infant before the first breath has been shown to decrease the incidence of respiratory distress syndrome. There are a number of surfactant preparations that have been approved by the U.S. Food and Drug Administration, including the synthetic preparations Exosurf, Survanta, and Infasurf, and the natural surfactant Curosurf. Both synthetic and natural surfactants have been shown to improve the incidence of respiratory distress syndrome by lessening the need for aggressive mechanical ventilation, less frequent pneumothorax, and decreased mortality.

The use of continuous positive airway pressure (CPAP) has been shown to improve oxygenation and ventilation of the preterm infant while minimizing ventilator associated lung injuries. Although many preterm infants will need continuous ventilator support, some studies show that the use of high-frequency oscillatory ventilation (HFOV) has shown some success in optimizing gas exchange in these preterm babies. Infants under 34 weeks’ gestational age in most neonatal centers are not candidates for extracorporeal membrane oxygenation (ECMO) secondary to intracranial hemorrhage. ECMO is reserved for children weighing more than 2000 grams and older than 34 weeks’ gestational age. High-frequency jet ventilation (HFJV) is another type of high-frequency ventilation that is very different than HFOV in that it delivers gases from a high-pressure source through a small bore cannula. It delivers rates from 150 to 600 and has demonstrated well in
CO₂ elimination. It has become a standard in treating IRDS patients with pulmonary interstitial emphysema (PIE).

**TREATMENT**

Treatment of IRDS is still controversial, but listed below are several methods that are shown to be beneficial:

- Surfactant replacement therapy (SRT)
- Continuous positive airway pressure (CPAP)
- High-frequency oscillatory ventilation (HFOV)
- High-frequency jet ventilation (HFJV)
- Administration of inhaled nitric oxide (iNO)
- Extracorporeal membrane oxygenation (ECMO)

Surfactant replacement therapy is the first line of defense in the treatment of IRDS. The amount of surfactant is determined by the patient’s weight; it is then warmed to body temperature and prepared for administration to the lungs via an endotracheal tube. The patient is intubated with an appropriate size endotracheal tube. Surfactant is delivered down either the endotracheal tube or through a side port attached to the endotracheal tube. The patient is manually resuscitated for several positive pressure breaths to get the surfactant to the periphery of the lung, or the patient is placed on the ventilator to provide positive pressure breaths; the latter is preferable because it provides consistent positive pressure breaths. The ventilator pressure is closely monitored so that it does not further damage the lungs. The respiratory therapist typically stays at the bedside to monitor the pressure being delivered by the ventilator. As lung compliance improves, the pressure is decreased in small increments, usually between 2 and 5 centimeters of water pressure. Some infant ventilators can now indicate compliance changes by monitoring volume changes. Care should be taken to not decrease the pressure too quickly. Once the optimal pressure is determined, the infant may be maintained on the ventilator; in some instances, the infant is extubated after a predetermined time and is transitioned to nasal CPAP.

Nasal CPAP is pressure, flow, and oxygen delivered continuously to the airway to maintain expansion of the alveoli and promote oxygen.
It can be delivered via a mechanical ventilator, the Infant Flow device made by Viasys Healthcare, or a heated, high-humidity nasal cannula (HHHNC; see Figure 2-1). High-humidity nasal cannula has been gaining ground in many nurseries as the alternative to mechanical ventilation. Some studies have shown that it is not comparable to the traditional CPAP and does not generate any increase in pressure for the infant while the infant’s mouth is opened; however, any device that delivers pressure to an infant with its mouth open will be inadequate. Additionally, the use of Vapotherm (see Figure 2-2) has also seen increased use in NICU. Other studies show that there is little to no difference in overall mortality between a group of infants with gestational age of 25 to 28 weeks ran-
domized to CPAP or intubation and ventilation. My personal experience with HHHNC has been successful, and in most instances I was able to prevent mechanical ventilation. A word of caution: The respiratory therapist will need to closely monitor the infant and be creative to prevent pressure and/or flows from escaping through the infant’s mouth.

High-frequency oscillatory ventilation uses a ventilator that operates with principles different from the conventional ventilators. A mean airway pressure (Paw) is created by delivering a bias flow past a resistance. This maneuver virtually creates CPAP, through a closed system via the endotracheal tube and the ventilator circuit, and is delivered to the lungs to help maintain lung volume. This pressure inflates the lung, minimizes the ventilation perfusion mismatch, and increases the alveolar surface area for gas exchange. This results in better oxygenation for the patient. There are lots of controversies surrounding high-frequency ventilation in the treatment of IRDS: some authors say that high-frequency ventilation is just as effective as conventional ventilation.

Inhaled nitric oxide administration is a selective pulmonary vasodilator and produces increased systemic oxygenation, with minimal side effects to the patient. It is beneficial in treating IRDS for those infants with PPHN. There is an increase in pulmonary vascular resistance, causing blood to shunt away from the lungs. Inhaled nitric oxide helps to lower pulmonary vascular resistance by promoting pulmonary vasodilation.

ECMO has been used in the treatment of IRDS when it manifests itself as PPHN and the condition is considered reversible. According to Philip Wolfson, the ECMO machine is a modified heart-lung machine that provides for gas exchange in a patient who is suffering from hypoxic respiratory failure. ECMO has been used successfully since 1974, treating more than 17,000 infants, with a survival rate of 78%. During the last few decades with the introduction of surfactant replacement therapy, inhaled nitric oxide, and better conventional ventilators, ECMO has been reserved for the most severe cases of infants with refractory hypoxemia.
SUMMARY

In spite of the advances in medical management, infant respiratory distress syndrome still occurs in 20,000 to 30,000 infants born each year in the United States. The introduction of surfactant therapy and better ventilator management strategy has significantly improved the mortality and morbidity of these infants. This chapter highlighted the following:

- Infants born before 37 weeks are at increase risk of infant respiratory distress syndrome, because of lack of surfactant production. Administration of surfactant prior to the infant’s first breath has been shown to be beneficial.
- Infants displaying meconium below the vocal cord are at risk for respiratory distress secondary to meconium aspiration syndrome. Aggressive suctioning below the vocal cords is the first line of therapy.
- Infants who are postterm, 24 hours to 48 hours postbirth, and display signs of grunting and retractions with respirations greater
than 60 are diagnosed with transient tachypnea of the newborn. This condition is self-limiting and is usually supported by oxygen therapy and careful monitoring.

✔ The condition in which an infant is born with a hole in his or her diaphragm that allows abdominal content into his or her chest wall is called congenital diaphragmatic hernia. This condition requires quick action to support the child’s oxygenation needs first.

✔ Postterm infants whose pulmonary vascular pressure remains high after birth are identified as having persistent pulmonary hypertension of the newborn. Infants born with meconium aspiration, transient tachypnea of the newborn, or congenital diaphragmatic hernia are at increased risk for PPHN due to the hypoxia insult to the lung tissue.

✔ Treatment of choice for preterm infants is surfactant therapy along with gentle positive pressure ventilation.

✔ Treatment of choice for postterm infants could be as simple as gentle positive pressure ventilation, inhaled nitric oxide, or high-frequency ventilation, and/or ECMO for the very severe case of IRDS.

REFERENCES

Chapter 2  Infant Respiratory Distress Syndrome (IRDS)


