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Newborn Respiratory Disorders

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Objectives

After completing this article, readers should be able to:

1. Evaluate and diagnose the most common causes of respiratory distress in the newborn period.
2. Differentiate between the normal results of a newborn chest radiograph and the radiographic patterns that reflect neonatal respiratory distress syndrome, meconium aspiration syndrome, retained fetal lung liquid syndrome, and neonatal pneumonia.
3. Recognize subglottic stenosis as a complication of endotracheal intubation.
4. Distinguish between pulmonary disease and cyanotic congenital heart disease as a cause of hypoxemia and acidosis in the neonate.
5. Discuss common complications of various respiratory disorders (such as meconium aspiration syndrome) and the untoward effects of specific therapies (intubation and mechanical ventilation).
6. Describe how chronic lung disease may result from meconium aspiration.

Introduction

Neonatal respiratory disorders account for most admissions to intensive care units in the immediate newborn period. Newborns in respiratory distress must be evaluated promptly and accurately; occasionally, neonatal respiratory distress is life-threatening and requires immediate intervention. The causes of respiratory distress in the newborn are numerous and are due to pulmonary or nonpulmonary processes. (1) Initial stabilization of the neonate, through management of the airway, breathing, and circulation, takes precedence over determining the cause. A thorough initial assessment, including maternal and neonatal history, physical examination, and appropriate use of diagnostic tests, is essential to diagnosing the cause of respiratory distress.

Abbreviations

ABG:	arterial blood gas
BPD:	bronchopulmonary dysplasia
CBC:	complete blood count
CLD:	chronic lung disease
CPAP:	continuous positive airway pressure
ECMO:	extracorporeal membrane oxygenation
Fio_2:	fraction of inspired oxygen
GBS:	group B *Streptococcus*
iNO:	inhaled nitric oxide
MAS:	meconium aspiration syndrome
NRP:	Neonatal Resuscitation Program
$Paco_2$:	partial pressure of arterial carbon dioxide
Pao_2:	partial pressure of arterial oxygen
RDS:	respiratory distress syndrome
RFLLS:	retained fetal lung liquid syndrome

Definition

Respiratory distress in the neonate most commonly presents as one or all of the following physical signs: tachypnea, grunting, nasal flaring, retractions, and cyanosis. (2) A normal respiratory rate in a newborn is between 30 and 60 breaths/min; tachypnea is classified as respiratory rates greater than 60 breaths/min. Patients born with surfactant deficiency and poorly compliant lungs have rapid, shallow breathing. Infants experiencing increased airway resistance, such as those who have subglottic stenosis, usually exhibit slower deep breathing (hyperpnea). Isolated tachypnea may be seen in congenital heart disease, but when accompanied by other signs of respiratory distress, tachypnea must be evaluated carefully to discern pulmonary from cardiac and metabolic causes. Grunting, a sound made on expiration against a partially closed glottis, produces elevated transpulmonary pressures and facilitates maintenance of functional residual capacity by stinting of the alveoli in a manner similar to applied continuous distending pressure. Grunting often is seen in disease states in which the alveoli are prone to collapse, such as surfactant deficiency. Nasal flaring results in a

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marked reduction in nasal resistance, which can reduce total lung resistance and decrease the work of breathing.

Retractions indicate a disturbance in lung and chest wall mechanics and are commonly observed in the intercostal, subcostal, and suprasternal muscles. Retractions become more apparent as the lung becomes less compliant, such as in surfactant deficiency. Severe retractions also can indicate airway obstruction.

Finally, cyanosis may be an advanced sign of respiratory distress. (3) Central cyanosis is defined as cyanosis of the mucous membranes and is more concerning than acrocyanosis, which can be a normal finding in a newly born infant. (3) Central cyanosis becomes clinically apparent when at least 5 g/100 mL of hemoglobin becomes unsaturated. (3) Clinical detection depends on the amount of desaturated hemoglobin present; in patients who have anemia or those who have larger amounts of fetal hemoglobin, cyanosis may not be detectable until the partial pressure of arterial oxygen (Pao_2) is very low. (4)

Assessment

Considering the complex series of cardiopulmonary changes that must occur for successful transition from intrauterine to extrauterine life, it is not surprising that newborns frequently present with respiratory distress soon after birth. Approximately 10% of babies require respiratory assistance immediately after delivery. Up to 1% require intensive resuscitation, which underlines the importance of having a person certified in the Neonatal Resuscitation Program (NRP) available for all deliveries and resuscitation equipment available in all delivery rooms. (2) Because there may be little time to gather the necessary history before stabilizing an infant in distress, initial assessment begins with a physical examination and assessment to identify any life-threatening conditions. In the immediate period following delivery, respiratory distress often is a consequence of the laboring process and resultant neonatal acidemia. Per NRP guidelines, effective ventilation with positive-pressure ventilation is indicated for all newborns who show evidence of apnea, gasping, ineffective respiratory effort, or heart rate of less than 100 beats/min. After stabilization per NRP guidelines, a number of diagnostic studies can be helpful in determining the cause of respiratory distress.

Initial diagnostic studies, especially a chest radiograph, should be ordered in newborns presenting with respiratory distress. Other helpful laboratory studies include serum glucose assessment, arterial blood gas (ABG) concentrations, complete blood count (CBC) with differential count, and blood culture. (3) After stabilization or assurance that the infant is stable from a respiratory standpoint, and once initial diagnostic studies have been ordered, a thorough history, both maternal and neonatal, should be taken.

Maternal history of medical disorders can be helpful in diagnosing the cause of neonatal respiratory distress. For example, a mother who has poorly controlled diabetes may have an infant susceptible to hypoglycemia, polycythemia, or relative surfactant deficiency, all of which can be responsible for neonatal respiratory distress. The history of the pregnancy also can be important. The estimated date of confinement can allow approximation of the infant's gestational age. A history of polyhydramnios can be concerning for tracheoesophageal fistula; oligohydramnios can be a sign of hypoplastic lungs. (3) Other helpful studies performed during pregnancy include the triple screen (maternal alpha-fetoprotein, human chorionic gonadotropin, and estriol), whose results can help assess the occurrence of genetic and developmental defects; prenatal ultrasonography; and a biophysical profile (measurement of fetal heart rate, muscle tone, movement, breathing, and amniotic fluid index). (2)

Information from fetal monitoring during labor and delivery as well as the presence of complications such as placenta previa or abruption, which can result in fetal anemia or hypovolemia, may indicate the underlying cause of respiratory distress. (3) Meconium in the amniotic fluid or trauma sustained during the birthing process may lead to respiratory distress. (3) The need for resuscitation in the immediate neonatal period and the circumstances surrounding the resuscitation also may provide clues to the diagnosis.

Finally, the history of the presentation can yield clues. For example, an infant who has initial respiratory distress that gradually improves with minimal intervention likely is suffering from retained fetal lung liquid syndrome (RFLLS). If the infant deteriorates gradually, the more likely diagnoses include pneumonia, respiratory distress syndrome (RDS), and sepsis. (2)

Repeated thorough physical examinations of the infant should follow stabilization and assessment. Vital signs are necessary in any objective examination and should be assessed frequently. (3) Temperature instability can be a sign of infection, and tachycardia may be a sign of hypovolemia. (3) It also is important simply to inspect the infant. Many of the signs of respiratory distress are seen rather than heard, including nasal flaring, retractions, and cyanosis. A scaphoid abdomen may be a sign of congenital diaphragmatic hernia. (2) Asymmetric chest movement might be a visual sign of tension pneumothorax. (3) Finally, the examiner should listen to the infant. Asymmetric breath sounds can be diagnostic of tension pneumothorax. Stridor, an expiratory

sound heard with upper airway obstruction, may represent subglottic stenosis in the previously intubated infant. (2) Assembling the information from the history, physical examination, and diagnostic studies should narrow the differential diagnosis considerably.

Differential Diagnosis

The differential diagnosis of respiratory distress in the newborn includes both pulmonary and nonpulmonary processes (Table 1). Common pulmonary causes include RFLLS, RDS, meconium aspiration syndrome (MAS), and pneumonia. (1) Nonpulmonary causes include cardiac disease, infection, metabolic disorders, central nervous system disorders, and several other miscellaneous disorders. (1)

Cardiac Disease Presenting as Newborn Respiratory Distress

Cyanotic congenital heart disease is a concerning nonpulmonary cause of respiratory distress that deserves prompt recognition. Heart disease commonly presents with central cyanosis, but the infant also may present with signs of heart failure. (2) Very few varieties of congenital heart disease present immediately after birth; often, they present several hours to days after delivery as the ductus arteriosus closes. The following five forms of congenital heart disease result in early respiratory distress on separation from the placental circulation: hypoplastic left heart syndrome with intact atrial septum, transposition of the great arteries with an intact ventricular septum and restrictive atrial septum, Ebstein anomaly of the tricuspid valve, tetralogy of Fallot with significant pulmonary stenosis or atresia, and obstructed total anomalous pulmonary venous return. It can be extremely difficult to differentiate between pulmonary disease and cardiac disease in a newborn who has respiratory distress, and it is important to remember that the two can coexist. (2) A cardiovascular examination revealing a hyperactive precordial impulse, gallop rhythm, poor capillary refill, weak pulses, decreased or delayed pulses in the lower extremities, or single second heart sound without splitting is more consistent with congenital heart disease. (2) The absence of a murmur does not distinguish between cardiac and pulmonary disease because murmurs are not present in many forms of congenital heart diseases. (5)

The definitive diagnostic test to rule in or out congenital heart disease is echocardiography, but this technology may not be readily available in all centers at all times. (5) It is important for the practitioner to use other tools to aid in diagnosis. A chest radiograph of the infant born with congenital heart disease may demonstrate abnormal pulmonary vasculature and a heart that is either enlarged

Table 1. Differential Diagnosis of Respiratory Distress in the Newborn (2)(3)

Upper Airway Obstruction
Choanal atresia, nasal stenosis, Pierre Robin syndrome, laryngeal stenosis or atresia, hemangioma, vocal cord paralysis, vascular rings, tracheobronchial stenosis, masses, cleft palate, nasal stuffiness
Pulmonary Diseases
Respiratory distress syndrome*, retained fetal lung liquid syndrome*, aspiration (including meconium aspiration syndrome)*, pneumonia*, pneumothorax, pneumomediastinum, primary pulmonary hypertension, tracheoesophageal fistula, pulmonary hemorrhage, pulmonary hypoplasia, pulmonary agenesis, cystic disease, pleural effusion, chylothorax, neoplasm, bronchopulmonary sequestration, pulmonary arteriovenous malformation, pulmonary interstitial emphysema, pulmonary edema, congenital alveolar proteinosis, congenital lobar emphysema
Cardiac Diseases
Cyanotic congenital heart disease*, acyanotic congenital heart disease*, arrhythmia, increased intravascular volume, high-output cardiac failure, pneumopericardium, cardiomyopathy
Thoracic Conditions
Chest wall deformity, mass
Metabolic Disorders
Hypoglycemia*, infant of a diabetic mother, inborn errors of metabolism, hypermagnesemia
Diaphragmatic Conditions
Hernia, paralysis
Neuromuscular Diseases
Central nervous system damage (birth trauma, hemorrhage), medication (maternal sedation, narcotic withdrawal), muscular disease (myasthenia gravis), intraventricular hemorrhage, meningitis, hypoxic-ischemic encephalopathy, seizure disorder, obstructed hydrocephalus, infantile botulism, spinal cord injury
Infectious Conditions
Sepsis*, pneumonia (especially group B *Streptococcus*)*
Hemolytic/Vascular Conditions
Anemia, polycythemia, abnormal hemoglobin
Miscellaneous
Asphyxia, acidosis*, hypo/hyperthermia, hypo/hypernatremia

*Common causes of respiratory distress in the newborn

or abnormally shaped. (3) ABGs of the newborn who has congenital heart disease typically reveal a normal partial pressure of arterial carbon dioxide ($Paco_2$) and a decreased Pao_2, and lung disease shows an increased $Paco_2$ and a decreased Pao_2. (3) Metabolic acidosis also may be present in response to low cardiac output and is more common in heart disease than in pulmonary disease. (2) Pulse oximetry can be used to attempt to differentiate between cardiac and lung disease. If oxygen saturations are less than 85% in room air and remain less than 85% in 100% fraction of inspired oxygen (Fio_2), most likely there is an intracardiac shunt. (1) If saturations increase to more than 85% in 100% Fio_2, a hyperoxia test should be performed to aid in the diagnosis. (1) In the hyperoxia test, a baseline right radial artery ABG (preductal) is obtained while the newborn is breathing room air and a second ABG is obtained from the same artery after the infant has been breathing 100% Fio_2. A Pao_2 of greater than 300 mm Hg is a normal result, a Pao_2 of greater than 150 mm Hg likely represents pulmonary disease, and a Pao_2 between 50 and 150 mm Hg represents cardiac disease or severe pulmonary hypertension. (1) Steps to help differentiate between cardiac disease and pulmonary disease are summarized in Table 2.

Retained Fetal Lung Liquid Syndrome

RFLLS generally is believed to be transient pulmonary edema that results from delayed clearance of fetal lung fluid. (2) At birth, the infant is presented with the challenge of rapidly clearing fluid that has filled the alveoli during gestation. During pregnancy, the lung epithelium is predominantly a secretory membrane; chloride pumps cause an influx of chloride and water from the interstitium into the alveolar space. (6) It is believed that fluid begins to clear the alveolar spaces about 2 to 3 days before the onset of labor, when the pulmonary epithelium becomes an absorbing membrane. (2) At that time, sodium becomes the predominant ion transported across the pulmonary epithelium, thereby reversing the direction of ion and water movement from the airspace to the interstitium. (7) Fluid in the interstitium subsequently is absorbed by the pulmonary lymphatics and vasculature. (6) About 40% of the fetal lung fluid is cleared before spontaneous vaginal delivery. For successful transition from intrauterine to extrauterine life, the rest of the fluid must clear within hours after birth. (7) Disruption of fluid clearance is implicated in the pathogenesis of RFLLS. (7)

RFLLS, initially described in 1966 by Avery and colleagues, presents with tachypnea, grunting, and nasal flaring immediately after birth. (2) It can occur in the term or preterm infant, affecting 3.6 to 5.7 per 1,000 term infants and up to 10 per 1,000 preterm infants. (6) Infant factors that increase the risk of RFLLS include male sex, delivery by cesarean section, perinatal asphyxia, and umbilical cord prolapse. (1) Maternal complications

Table 2. Differentiation of Cyanotic Heart Disease from Pulmonary Disease in Respiratory Distress*

	Cyanotic Heart Disease (CHD)	Pulmonary Disease
History	• Previous sibling having CHD • CHD diagnosed on prenatal ultrasonography	• Cesarean section without labor • Preterm birth • Meconium-stained amniotic fluid • Maternal fever
Physical Examination	• Cyanosis • Single second heart sound • Gallop rhythm • Weak lower extremity pulses • Quiet tachypnea	• Cyanosis • Split second heart sound • Retractions • Temperature instability • Crackles (rales), rhonchi
Chest Radiograph	• Increased heart size • Abnormal heart shape • Abnormal pulmonary vasculature	• Normal heart size • Abnormal pulmonary parenchyma
Arterial Blood Gases	• Normal or decreased $Paco_2$ • Decreased Pao_2	• Increased $Paco_2$ • Decreased Pao_2
Hyperoxia Test	• Pao_2 50 to 150 mm Hg	• Pao_2 >150 mm Hg
Echocardiography	• Abnormal heart and vessels	• Normal heart and vessels

$Paco_2$=partial pressure of arterial carbon dioxide, Pao_2=partial pressure of arterial oxygen
*Adapted from Aly (2).

that can increase risk include asthma, diabetes, and need for analgesia or anesthesia during labor. (1)

The definitive diagnosis of RFLLS is based on resolution of symptoms within 1 to 5 days after minimal therapeutic intervention. (6) Chest radiographs can support the diagnosis and classically are characterized by prominent perihilar streaking, increased interstitial markings, and fluid in the interlobar fissures (Fig. 1). (6) There may be a "wet silhouette" around the heart as well as signs of alveolar edema. (1)(2) Usually, there is diffuse involvement in the lungs, which can make RFLLS difficult to distinguish radiographically from RDS, and a coarse interstitial pattern that may resemble pulmonary edema or irregular opacifications may cause RFLLS to appear as MAS or neonatal pneumonia. (1) Blood gas analysis in RFLLS reveals a respiratory acidosis with mild-to-moderate hypoxemia. (2)

Treatment of RFLLS is supportive. The disorder usually responds to oxygen therapy, but maintaining appropriate oxygen saturation may require continuous positive airway pressure (CPAP). (2) CPAP can aid in increasing the distending pressure of the alveoli and the absorption of the extra lung fluid. (2) Supplemental oxygen should be administered to keep oxygen saturations in normal ranges; at times, high concentrations of oxygen are necessary. (6) Very rarely is mechanical ventilation necessary. (2) RFLLS usually is a benign and self-limited disease, and typically there are no long-term sequelae. (2)

Respiratory Distress Syndrome

RDS is caused by surfactant deficiency and, therefore, is primarily a disease of prematurity. (1) In fact, the risk of RDS decreases with increasing gestational age, with at least 60% of babies born at less than 28 weeks' gestation, approximately 30% of babies born at less than 30 weeks' gestation, and fewer than 5% of babies born at term developing RDS. (8) Surfactant is a mixture of lipids and proteins produced by type II pneumocytes in the lung epithelium. (9) The absence of surfactant in the liquid film lining of the alveoli causes an increase in surface tension and alveolar collapse. (9) If not treated, such atelectasis leads to increased work of breathing, intrapulmonary shunting, ventilation-perfusion mismatch, hypoxia, and eventual respiratory failure. (10)

In addition to prematurity, other factors that increase the risk of RDS include male sex, maternal gestational diabetes, perinatal asphyxia, hypothermia, and multiple gestations. (11) Infants who develop RDS present with signs of respiratory distress at the time of or soon after birth that worsen over time. (9)

Along with the history and physical examination, a chest radiograph is considered necessary for diagnosing RDS. Diffuse microatelectasis is present on the chest film, giving the classic "ground glass" appearance of the lungs, (9) with resultant diminished overall lung volume. Air bronchograms, which are air-filled bronchi superimposed on the relatively airless parenchyma of the lung tissue, also are seen commonly on chest radiograph (Fig. 2). (9) ABG measure-

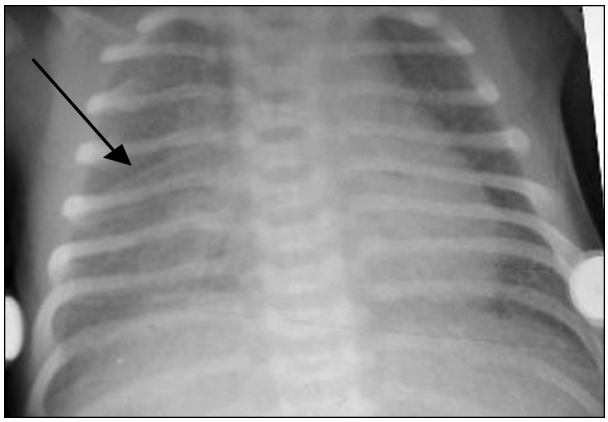

Figure 1. Retained fetal lung liquid syndrome. Note the increased interstitial markings and fluid in the interlobar fissure on the right (arrow).

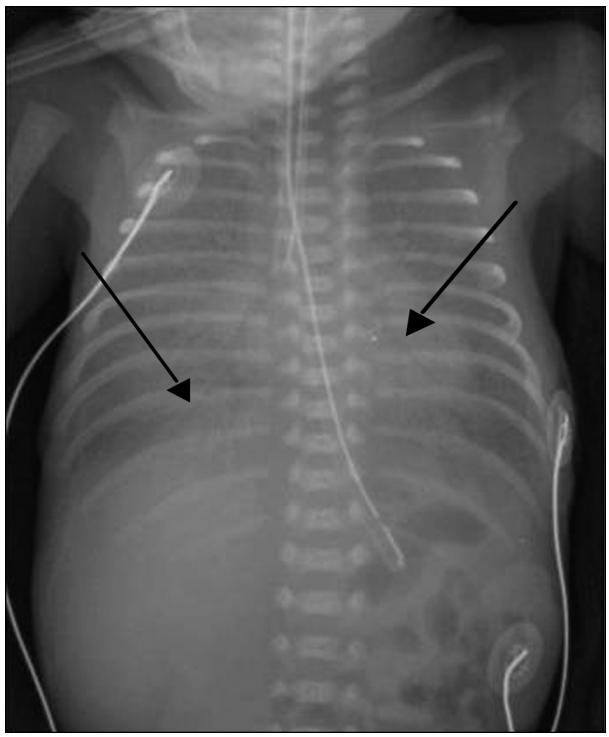

Figure 2. Respiratory distress syndrome. Note the "ground glass" appearance, which represents diffuse microatelectasis, and air bronchograms (arrows).

ments demonstrate hypercarbia and hypoxia and eventually, in the unsupported infant, metabolic acidosis. (9)

Treatment of RDS begins antenatally with the administration of corticosteroids to women at risk for preterm delivery before 34 weeks' gestation, therapy that has constituted standard practice since the 1994 National Institutes of Health Consensus Conference. (12) Antenatal corticosteroids decrease the risk of RDS by accelerating fetal lung maturation. (12) Postnatally, surfactant replacement therapy has been approved for use since 1990 and provides almost immediate improvement in oxygenation for surfactant-deficient infants. (8) Surfactant replacement therapy continues to be an area of active research, including the use of natural versus synthetic surfactants, prophylactic versus selective administration, and single versus multiple doses.

Mechanical ventilation often is necessary in infants affected by RDS; nasal CPAP also has been shown to be effective in maintaining lung volumes in surfactant-deficient lungs. Many centers now have begun to use a strategy of intubation and surfactant administration, followed by extubation and minimally invasive respiratory support (such as nasal CPAP), a regimen that has proven to be safe and effective. (13)

The major complications and long-term sequelae of RDS are associated principally with the treatments. Bronchopulmonary dysplasia (BPD), characterized by the need for oxygen supplementation at 36 weeks' corrected gestational age, likely results from high levels of oxygen administration and mechanical ventilation. (14)

Meconium Aspiration Syndrome

MAS is defined as respiratory distress in an infant born through meconium-stained amniotic fluid whose symptoms cannot otherwise be explained. (1) Among all live births, 13% are complicated by meconium-stained amniotic fluid, and of these infants, 4% to 5% develop MAS. (1) Most infants affected by MAS are term or postterm because they naturally pass meconium before birth due to maturation of the gastrointestinal tract. (15) A fetus passing meconium in utero usually is a sign of fetal stress and hypoxemia that led to relaxation of the anal sphincter. (15)(16) Any factor that results in fetal stress can be a risk factor for passing meconium in utero, including maternal hypertension, maternal diabetes, eclampsia, and many others. (15) Chronic fetal hypoxia and acidosis can lead to gasping in utero and aspiration of meconium. (15) Evidence suggests that chronic in utero meconium aspiration is probably the cause of the most severe cases of MAS. (15)

Severe MAS is associated with alterations in the pulmonary vasculature, including remodeling and thickening of the muscular walls. This process results in pulmonary vascular hyperreactivity, vasoconstriction, and hypertension. Those more vigorous infants who aspirate meconium through the nasopharynx at the time of birth are more likely to develop mild-to-moderate MAS. (15)

Meconium is directly toxic to the lungs. Meconium consists of water, desquamated cells from the gastrointestinal tract, skin, lanugo hair, vernix, bile salts, pancreatic enzymes, lipids, and mucopolysaccharides. (2) The bile salts and pancreatic enzymes, along with some of the other components, can cause a chemical pneumonitis, one aspect of MAS. (3) Meconium also inactivates surfactant by displacing it from the alveolar surface and inhibiting its surface tension-lowering ability. (15) Meconium activates the complement cascade, which leads to inflammation and vasoconstriction of the pulmonary veins. (1) Finally, the thick, particulate meconium itself can cause partial-to-complete airway obstruction. (1)

Infants who develop MAS typically present in the first 12 hours after birth with varying degrees of respiratory distress. (15) On inspection, many affected infants have "barrel chests," and crackles (rales) and rhonchi often can be heard on auscultation. (2) The chest radiograph of an infant who has MAS varies with the severity of meconium aspiration. (1) Typically, radiographs demonstrate areas of patchy atelectasis due to complete airway obstruction, with other areas of overinflation due to the air trapping seen with partial obstruction and subsequent development of a one-way valve phenomenon (Fig. 3). (1) Widespread involvement of all lung fields is seen, and in the most severe cases,

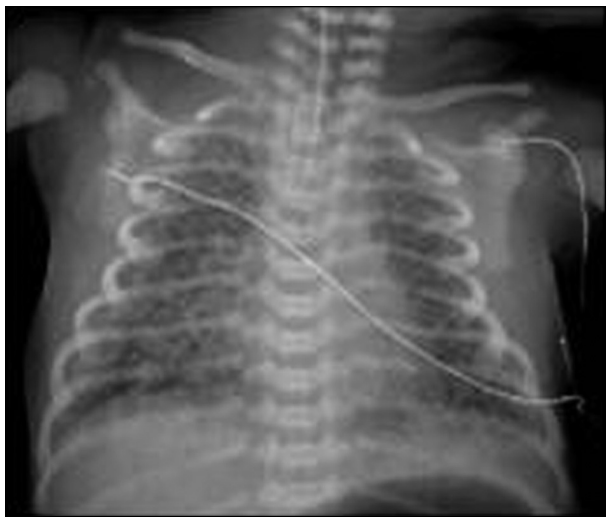

Figure 3. Meconium aspiration syndrome. Note the areas of patchy atelectasis combined with the areas of overinflation due to air trapping.

there may be an almost total whiteout of the lungs, with only large bronchi distinguishable. (1)

Due to the extreme overinflation, secondary pulmonary air leaks on chest radiograph also are common. (15) Such air leaks include pneumothorax, seen in 10% to 20% of affected infants; pulmonary interstitial emphysema; and pneumomediastinum. (1)(2) Normalization of chest radiographs after resolution of MAS may take days to weeks. (15)

The treatment of MAS has evolved over the years. Amnioinfusion, which is the infusion of isotonic fluid into the amniotic cavity via catheter before delivery, was believed to be a reasonable treatment for meconium-stained amniotic fluid at one time to try to prevent aspiration of meconium in the birthing process. (1) However, subsequent randomized, controlled trials have found that amnioinfusion provides no significant benefit. (16) Similarly, suctioning of the mouth, nose, and nasopharynx after delivery of the head and before delivery of the shoulders previously was undertaken on every infant born through meconium-stained amniotic fluid. (16) NRP guidelines now state that no intervention should be undertaken during delivery in the presence of meconium-stained fluid. If the infant is vigorous, as defined by strong respiratory effort, heart rate greater than 100 beats/min, and good muscle tone, bulb syringe suctioning of the mouth should be performed after delivery, followed by standard NRP procedures. If the infant is not vigorous, the mouth and trachea should be suctioned before proceeding with NRP recommendations. (16)

For those infants who develop more severe MAS, transfer to a center capable of providing surfactant, inhaled nitric oxide (iNO), and extracorporeal membrane oxygenation (ECMO) is necessary. Surfactant replacement therapy has become more standard for infants suffering from MAS because surfactant inactivation is a known result of acquiring intra-alveolar meconium. Randomized, controlled trials have shown a decreased need for ECMO therapy and, perhaps, a lower rate of pneumothorax in infants treated with surfactant. (1)

Approved for use by the United States Food and Drug Association in 2001, iNO has become a standard treatment for MAS. (1) Because meconium also causes vasoconstriction of the pulmonary vessels, iNO can ameliorate the pulmonary hypertension that accompanies MAS by its ability to vasodilate the pulmonary capillaries selectively. (15) Treatment with iNO results in a better ventilation-perfusion match and decreases the need for ECMO in infants who have MAS. (15)

High-frequency ventilation strategies have become popular for use in infants who have MAS because this method inflicts less barotrauma to the lungs. (15) However, no randomized, controlled trials have compared the use of conventional ventilation to high-frequency ventilation in this population. (15) Finally, ECMO is used in infants who have MAS and who fail iNO therapy. Up to 40% of infants who require iNO also need ECMO. (15) Of note, infants who have MAS and require ECMO tend to have survival rates of up to 93% to 100%. (15)

A major condition associated with MAS is pulmonary hypertension. The chemical pneumonitis and surfactant inactivation that result from meconium injury lead to inadequate ventilation after birth and impaired pulmonary transition. (11) This situation, in combination with the release of pulmonary vasoconstrictors, leads to the pulmonary hypertension seen in MAS. (17) Treating infants who have MAS often requires harsh ventilator therapy that can result in chronic lung disease (CLD). However, improving oxygenation should be emphasized because hypoxemia increases pulmonary vascular resistance that, in turn, worsens pulmonary hypertension. (17)

Pneumonia

Pneumonia is the most common infection in the neonate and is a significant cause of respiratory distress in newborns. (2) Pneumonia may develop in the antenatal, perinatal, or postnatal period, and the cause varies according to when the infection develops. (1) Rubella, herpes simplex virus, cytomegalovirus, adenovirus, *Toxoplasma gondii*, varicella-zoster virus, and several other pathogens contracted in the intrauterine period can cause pneumonia. (1) Perinatally acquired bacteria that cause pneumonia include group B *Streptococcus* (GBS), *Escherichia coli*, *Klebsiella*, and *Chlamydia trachomatis*. (1) Pneumonia acquired in the post-

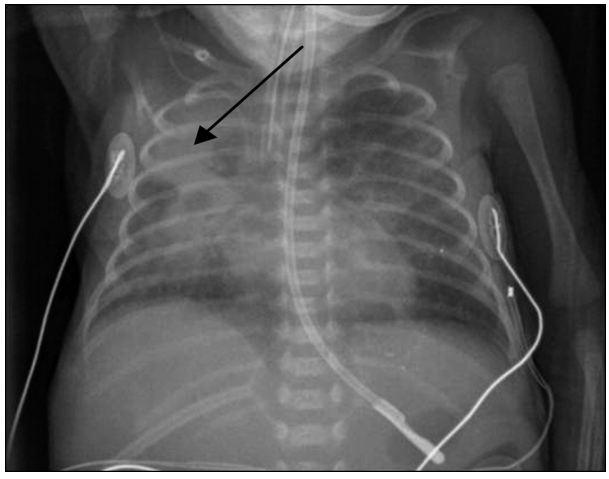

Figure 4. Neonatal pneumonia. Note the right upper lobar consolidation (arrow).

Table 3. Comparative Chest Radiograph Findings in Neonatal Respiratory Distress

	RFLLS	RDS	MAS	Pneumonia
Diffuse parenchymal infiltrates	X		X	X
Air bronchograms		X		X
Lobar consolidation				X
Patchy areas alternating with emphysema			X	
Pleural effusion				X
Reticular granular pattern		X		X
Loss of lung volume		X	X	
Fluid accumulation in interlobar spaces	X			
Hyperinflation	X		X	
Atelectasis		X	X	
Pneumothorax/Pneumomediastinum		X	X	X

MAS=meconium aspiration syndrome, RDS=respiratory distress syndrome, RFLLS=retained fetal lung liquid syndrome
*Adapted from Flidel-Rimon & Shinwell, 2005.

natal period may be caused by respiratory viruses, gram-positive bacteria (groups A, B, and G streptococci or *Staphylococcus aureus*), and gram-negative bacteria (*Klebsiella*, *Proteus*, *Pseudomonas aeruginosa*, *Serratia marcescens*, and *E coli*). (1)

Signs exhibited by infants who have pneumonia include any of the signs of respiratory distress, thus sometimes making pneumonia very difficult to distinguish from RFLLS, RDS, or MAS. (3) Signs typically present in the first several hours after birth unless the pneumonia is acquired postnatally. (3) Other signs and symptoms may include lethargy, poor feeding, jaundice, apnea, and temperature instability. (2)

Table 4. When to Call a Neonatologist for Respiratory Distress in an Infant

- Stabilization of the infant in respiratory distress is challenging
- Heart disease is suspected and echocardiography or medications (such as prostaglandins) are not available
- Need for respiratory support, supplemental oxygen, or medications beyond what is available at the institution
- Concerns for evolving pulmonary hypertension, especially in an infant who has meconium aspiration syndrome
- Concerns for evolving sepsis in an infant who has pneumonia
- Inability to ventilate
- Pulmonary hemorrhage
- Persistent or progressing pneumothorax

If pneumonia is suspected, initial screening tests, including CBC with differential count and blood culture, should be obtained before beginning antibiotic therapy. (3) Ampicillin and gentamicin are the antibiotics used most frequently in the neonatal period for treating infection. (18) The chest radiograph of the infant who has pneumonia varies, depending on the cause. In utero infection typically

Summary

- Respiratory distress presents with any or all of the following findings: tachypnea, grunting, nasal flaring, retractions, and cyanosis.
- Respiratory distress can be pulmonary or nonpulmonary, stabilization is paramount, and diagnosis is aided by history and physical examination as well as diagnostic tests.
- Cyanotic congenital heart disease, an important cause of neonatal respiratory distress, must be recognized promptly.
- RFLLS probably is caused by a delay in the clearance of fetal lung fluid and is usually a benign, self-limited illness.
- RDS occurs primarily in preterm infants as a result of surfactant deficiency; based on strong research evidence, the use of antenatal corticosteroids reduces the incidence of RDS (12) and use of postnatal surfactant is an effective treatment. (8)
- Severe MAS may require harsh ventilatory support that can result in CLD; strong research evidence shows that surfactant administration (1) and iNO use (15) both decrease the need for ECMO in infants who have pulmonary hypertension related to MAS.
- Neonatal pneumonia can be acquired antenatally, perinatally, or postnatally, and causes vary, depending on the timing of disease acquisition.

manifests as bilateral consolidation or "whiteout." (2) Other pneumonias can manifest as lobar consolidations on chest radiograph (Fig. 4). (2) GBS pneumonia is easy to confuse with other causes of respiratory distress when looking at the chest radiograph. For example, 50% of infants who have GBS pneumonia have radiographic findings indistinguishable from those of RDS or RFLLS. (18) When present, pleural effusion or mild heart enlargement in the absence of cardiac anomalies suggests the diagnosis of pneumonia. (1)

Treatment of pneumonia focuses on supportive care of the infant and administration of antibiotic medications that target the causative organism. (1) Oxygen therapy, mechanical ventilation, and vasopressor administration may be necessary. (1) Oxygen should be used to maintain saturations in the normal ranges for gestational age.

Table 3 compares chest radiograph findings in RFLLS, RDS, MAS, and pneumonia, and Table 4 lists recommended reasons for consulting a neonatologist.

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PIR Quiz

Quiz also available online at http://pedsinreview.aappublications.org.

1. A newborn male develops respiratory difficulty 4 hours after birth. His estimated gestational age is 30 weeks. Respirations are 65 breaths/min and shallow, heart rate is 130 beats/min, and blood pressure is 60/30 mm Hg. He exhibits nasal flaring, intercostal and subcostal retractions, and grunting. His nail beds and lips appear dusky. A pulse oximetry reading shows an oxyhemoglobin saturation of 78% in room air and 92% in 60% oxygen hood. A chest radiograph shows a diffuse reticulogranular pattern, air bronchograms, and decreased lung volume. Which of the following is the *most* likely explanation for his respiratory distress?

   A. Decreased chest wall compliance
   B. Delayed clearance of amniotic fluid.
   C. Increased airway resistance.
   D. Increased alveolar surface tension.
   E. Persistent pulmonary hypertension.

2. A 12-hour-old girl appears cyanotic and is breathing rapidly. She was born after a term spontaneous vaginal delivery. Amniotic fluid was stained with meconium. Physical examination reveals a respiratory rate of 66 breaths/min, heart rate of 130 beats/min, and blood pressure of 72/42 mm Hg. Mild intercostal and subcostal retractions are noted. Pulses are equal in all extremities. Lips and nail beds are cyanotic. Chest auscultation reveals clear breath sounds, a single second heart sound, and no heart murmur. Chest radiograph shows clear lung fields. Pulse oximetry reveals an oxyhemoglobin saturation of 70% in room air and 75% in 100% Fio_2. Which of the following is the *most* likely diagnosis?

   A. Hypoplastic left heart syndrome.
   B. Meconium aspiration syndrome.
   C. Persistent pulmonary hypertension of the newborn.
   D. Pulmonary atresia.
   E. Retained fetal lung liquid syndrome.

3. A 1-hour-old boy develops rapid respirations. He was born after 39 weeks' gestation and delivered by elective cesarean section. His mother had two other children delivered by cesarean sections for cephalopelvic disproportion. Apgar scores were 8 and 9 after 1 and 5 minutes, respectively. The infant is vigorous and responds appropriately to stimulation. The respiratory rate is 70 breaths/min, heart rate is 120 beats/min, and blood pressure is 72/40 mm Hg. Pulses are equal in all extremities. Nasal flaring, grunting, and intercostal retractions are noted. Chest auscultation reveals normal breath sounds and a split second heart sound. Pulse oximetry monitoring shows an oxyhemoglobin saturation of 88% in room air and 96% in 40% oxygen hood. Chest radiography shows prominent perihilar streaking and fluid in the interlobar fissures. Which of the following is the *most* appropriate management at this time?

   A. Continuation of current therapy and observation.
   B. Echocardiography evaluation.
   C. Hyperoxia test with radial artery blood gas determination.
   D. Intubation and inhaled nitric oxide therapy.
   E. Intubation and instillation of surfactant.

4. You are called to attend the delivery of a term baby. The membranes ruptured 1 hour ago, and the amniotic fluid is meconium-stained. The head is fully engaged. Which of the following is the *most* appropriate strategy in managing this situation?

   A. If the infant remains vigorous after delivery, suction the mouth only with bulb syringe.
   B. Infuse isotonic saline in the amniotic cavity via a catheter before delivery.
   C. Recommend that cesarean section be performed immediately.
   D. Suction the mouth, nose, and nasopharynx as soon as the head is delivered.
   E. View the glottis and suction the trachea after delivery regardless of how the infant appears.

Newborn Respiratory Disorders
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