Respiratory Distress in the Term and Near-term Infant
Orna Flidel-Rimon and Eric S. Shinwell
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Objective. After completing this article, readers should be able to:

1. Differentiate between cardiac and respiratory causes of cyanosis.
2. Describe the primary parenchymal diseases that can cause respiratory distress in the neonate.
3. Describe the primary developmental lung abnormalities that can cause respiratory distress in the neonate.

Introduction

One of the most common reasons for admission of term neonates to a neonatal intensive care unit (NICU) is respiratory distress. (1) The cause may be of pulmonary or nonpulmonary origin. The nonpulmonary causes include cardiac, infectious, metabolic, central nervous system, and miscellaneous conditions. This review focuses on the major pulmonary causes for respiratory distress in term infants, in particular, the first two of the four groups that appear in Table 1. (2)

Rule Out Cardiac Disease

Differentiating cardiac and respiratory causes of cyanosis is a common clinical problem, particularly in cases in which there is little or no tachypnea or respiratory distress. The major signs of neonatal respiratory distress are tachypnea and cyanosis, in which tachypnea is defined as a respiratory rate consistently greater than 60 breaths/min. A hyperoxia test may assist in differentiating between the two. Pulse oximetry may help to decide whether a formal hyperoxic test is useful. A neonate who exhibits cyanosis without marked respiratory distress and has an O₂ saturation of less than 85% in both room air and 100% oxygen likely has an intracardiac shunt. If the O₂ saturation increases to more than 85% on 100% oxygen, a full hyperoxia test should be performed. The test consists of obtaining a baseline right radial (preductal) arterial blood gas measurement with the child breathing room air and repeating the measurement while the infant is receiving 100% O₂. A PaO₂ measurement greater than 300 mm Hg on 100% oxygen is normal, more than 150 mm Hg suggests pulmonary disease, and 50 to 150 mm Hg suggests cardiac disease (or severe pulmonary hypertension). (3) Echocardiography is the definitive investigation, but because it is not immediately available in most units at all hours of the day and night, it is important for the clinician to be familiar with the previously noted initial approach.

Hints on the Chest Radiograph

For respiratory distress caused by parenchymal disorders, the standard chest radiograph remains the most common and useful imaging tool. (4) The location of the stomach, liver, and heart should be determined to rule out dextrocardia and situs inversus. The spectrum of diseases that affect the neonate’s chest have significant overlap in their radiographic and clinical appearances, such that an open exchange of information between the neonatologist and radiologist is critical for intelligent interpretation of the radiologic images in conjunction with the clinical picture. The following is a brief overview of possible diagnostic clues (see also Table 2).

In term (rare) or near-term infants who have respiratory distress syndrome (RDS), the maximum radiographic findings may not be present until 24 to 48 hours after birth. The
characteristic reticular granular pattern and air bronchograms may develop as the infant uses existing surfactant stores in advance of adequate endogenous production. In addition, exogenous surfactant therapy alters the natural course of the radiographic findings. Because the surfactant may not be distributed evenly throughout the lungs, areas of aerated lung may alternate with areas of unchanged RDS. In addition, surfactant can cause excessive distention of multiple acinar units, resulting in pulmonary interstitial emphysema on the chest radiograph. Although this usually resolves spontaneously, it may be a harbinger of other pulmonary air leaks, such as pneumothorax.

In neonatal pneumonia, the chest radiograph may reveal classical patchy infiltrates, but the findings also may be indistinguishable from RDS. The presence of a pleural effusion supports the diagnosis of pneumonia; it has been reported in up to 67% of cases, but essentially never in uncomplicated RDS. Mild cardiac enlargement in the absence of cardiac anomalies also is seen more often in pneumonia than in RDS.

The radiographic findings in meconium aspiration syndrome (MAS) vary with the severity of the aspiration. The typical chest film shows patchy areas of atelectasis due to complete airway obstruction, interspersed with areas of air trapping due to partial obstruction and a one-way valve phenomenon. There is usually widespread involvement, with no particular area of the lungs being affected more often. In severe disease, there may be an almost total white-out, with only large bronchi distinguishable. Secondary pulmonary air leaks such as pneumothorax, pulmonary interstitial emphysema, or pneumomediastinum frequently are seen.

Transient tachypnea of the newborn (TTN) is characterized by the presence of diffuse parenchymal infiltrates, a “wet silhouette” around the heart, or accumulation of fluid in the various intralobar spaces that indicate increased pulmonary interstitial, alveolar, or pleural water content. The lungs usually are affected diffusely, and sometimes it may be difficult to distinguish TTN from RDS. Similarly, in some cases of TTN, a coarse interstitial pattern may appear similar to pulmonary edema or an irregular opacification may be similar to MAS or neonatal pneumonia. Transient slight cardiac enlargement may occur.

In congenital lymphangiectasia, the lungs may appear normal or exhibit a coarse interstitial infiltrate due to the distended, abnormal lymphatics. There may be generalized overinflation. Pleural effusion may be seen in lymphangiectasia and in traumatic, chylous, or hemorrhagic effusion.

Table 1. Potential Pulmonary Causes for Respiratory Distress in Neonates

<table>
<thead>
<tr>
<th>Parenchymal conditions</th>
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<tbody>
<tr>
<td>Transient tachypnea of the newborn</td>
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<tr>
<td>Meconium aspiration syndrome and other aspirations</td>
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<tr>
<td>Respiratory distress syndrome</td>
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<tr>
<td>Pneumonia</td>
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<tr>
<td>Pulmonary edema</td>
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<tr>
<td>Pulmonary hemorrhage</td>
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<td>Pulmonary lymphangiectasia</td>
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<tr>
<th>Developmental abnormalities</th>
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<tr>
<td>Lobar emphysema</td>
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<tr>
<td>Pulmonary sequestration</td>
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<tr>
<td>Cystic adenomatoid malformation</td>
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<tr>
<td>Congenital diaphragmatic hernia</td>
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<tr>
<td>Tracheoesophageal fistula</td>
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<td>Pulmonary hypoplasia</td>
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<table>
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<tr>
<th>Airway abnormalities</th>
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<tbody>
<tr>
<td>Choanal atresia/stenosis</td>
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<tr>
<td>Laryngeal web</td>
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<tr>
<td>Laryngotraceomalacia or bronchomalacia</td>
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<tr>
<td>Subglottic stenosis</td>
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<tr>
<th>Mechanical abnormalities</th>
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<tbody>
<tr>
<td>Rib cage anomalies (eg, Jeune syndrome)</td>
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<tr>
<td>Pneumothorax</td>
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<tr>
<td>Pneumomediastinum</td>
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<tr>
<td>Pleural effusion</td>
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<tr>
<td>Chylothorax</td>
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More Imaging Modalities

Computed tomography (CT) scan may be useful in confirming the presence of the lung lesions, determining the extent of the lesion, and defining the associated abnormalities. (5) Reconstructed data from CT examination displayed in either three-dimensional or multiplanar formats are particularly helpful in delineating abnormalities of the bronchi and of arterial and venous structures. (6)

Continuous sophisticated imaging techniques such as high-resolution ultrasonography and ultrafast magnetic resonance imaging enable intrauterine definition of certain lesions.

In congenital diaphragmatic hernia (CDH), two important features that determine the prognosis are herniation of the liver into the chest and the lung-to-head proportion.
circumference ratio (LHR). Liver herniation may be determined sonographically by Doppler evaluation of the abnormal course of the umbilical, hepatic, and portal veins. The LHR estimates the volume of the contralateral lung, thereby providing a measure of the expected degree of pulmonary hypoplasia. When the LHR is less than 0.9, the outcome is usually poor; when it is greater than 1.4, a good outcome is more likely. (7) This information may influence parents to consider delivering at a center that has advanced therapeutic modalities, such as extracorporeal membrane oxygenation (ECMO).

Congenital lobar emphysema may be detected in utero as an echogenic mass on ultrasonography, with associated mediastinal shift and displacement of the heart resulting in compression of the contralateral lung. Fetal ultrasonography may diagnose extralobar emphysema as early as 19 weeks of gestation. (6)

### Parenchymal Diseases

**TTN**

TTN initially was described by Avery and colleagues in 1966. (8) This relatively benign, self-limited disease also is known as RDS type 2 or wet lungs. It occurs in approximately 11 per 1,000 live births and appears more often in boys, in infants delivered by cesarean section, and in infants who have perinatal asphyxia, umbilical cord prolapse, or maternal complications such as asthma, diabetes, or analgesia or anesthesia during labor. The syndrome is characterized by tachypnea that appears shortly after birth and usually clears within 1 to 5 days. The precise cause is unknown, but it is believed to be due to delayed resorption of fetal lung fluid that may be related to elevated central venous pressure and delayed clearance of pulmonary fluid by the lymphatics. The reason for the delayed absorption is unknown, but it has been suggested to be attributed to mild asphyxia resulting in mild pulmonary capillary leak and to myocardial dysfunction with elevated filling pressure. (9) In most cases, the clinical course is benign, and mechanical ventilation almost never is required.

**RDS**

Although RDS is primarily a disease of preterm infants, some near-term infants may be affected. These infants are typically 34 to 37 weeks of gestation, and risk factors include maternal diabetes, multiple birth, cesarean section prior to the onset of labor, perinatal asphyxia, cold stress, and infants whose siblings suffered from RDS. Because their surfactant sufficiency is borderline and they have larger pulmonary reserves, affected infants may be able to cope without ventilation for longer than smaller preterm infants. Infants who have RDS may do well with nasal continuous positive airway pressure or may require mechanical ventilation.

### Table 2. Possible Diagnoses Related to Radiographic Features

<table>
<thead>
<tr>
<th>Radiographic Features</th>
<th>Possible Diagnosis</th>
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<tbody>
<tr>
<td>Air bronchograms</td>
<td>• RDS</td>
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<tr>
<td>Diffuse parenchymal infiltrates</td>
<td>• RDS</td>
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<tr>
<td>• Pneumonia</td>
<td></td>
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<tr>
<td>• TTN</td>
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<td>• MAS</td>
<td></td>
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<tr>
<td>• Pneumonia</td>
<td></td>
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<tr>
<td>• Pulmonary lymphangiectasia</td>
<td></td>
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<tr>
<td>Lobar consolidation</td>
<td>• Pneumonia</td>
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<tr>
<td>• Lobar sequestration</td>
<td>• CCAM</td>
</tr>
<tr>
<td>Patchy areas alternating with emphysema</td>
<td>• MAS</td>
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<tr>
<td>Pleural effusion</td>
<td>• Pneumonia</td>
</tr>
<tr>
<td>• Pulmonary lymphangiectasia</td>
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<tr>
<td>Reticular granular pattern</td>
<td>• Pneumonia</td>
</tr>
<tr>
<td>Loss of lung volume</td>
<td>• RDS</td>
</tr>
<tr>
<td>Fluid accumulations in interlobar spaces</td>
<td>• TTN</td>
</tr>
<tr>
<td>• Pulmonary lymphangiectasia</td>
<td></td>
</tr>
<tr>
<td>Hyperinflation</td>
<td>• TTN</td>
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<tr>
<td>• Pulmonary lymphangiectasia</td>
<td></td>
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<tr>
<td>Atelectasis</td>
<td>• MAS</td>
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<tr>
<td>• Pneumonia</td>
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<tr>
<td>Pneumothorax/pneumomediastinum</td>
<td>• Spontaneous</td>
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<tr>
<td>• MAS</td>
<td></td>
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<tr>
<td>• RDS</td>
<td></td>
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<tr>
<td>• Pneumonia</td>
<td></td>
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<tr>
<td>“Cystic” mass</td>
<td>• CCAM</td>
</tr>
<tr>
<td>• CDH</td>
<td></td>
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<tr>
<td>• Pulmonary sequestration</td>
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RDS = respiratory distress syndrome, TTN = transient tachypnea of the newborn, MAS = meconium aspiration syndrome, CCAM = congenital cystic adenomatoid malformation, CDH = congenital diaphragmatic hernia.

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ventilation. Surfactant often improves pulmonary mechanics significantly but has little effect on overall outcome, which is favorable in most cases. (10)  

**Abnormalities of Surfactant Proteins**  
A small but notable group of term infants who have severe respiratory distress have congenital abnormalities of surfactant proteins. The most common of these conditions is deficiency of surfactant protein B (SP-B). Affected infants develop severe respiratory distress shortly after birth, and chest radiographs show findings identical to those of RDS. However, infants who have deficiency of SP-B continue to suffer from extreme respiratory insufficiency despite mechanical ventilation, oxygen, repeated surfactant replacement therapy, and corticosteroids. The only effective therapy (although neither available for nor consented to by all) is lung transplantation, without which the infants die within 1 to 6 months.  

SP-B deficiency is transmitted as an autosomal recessive trait and is fatal in homozygotes; heterozygotes are clinically asymptomatic. Compound heterozygotes (two different mutant alleles at the same loci) have a milder form of the disease. The gene for SP-B is located on chromosome 2 and comprises 11 exons. The most common defect (60 to 70%) in the SP-B gene is a frame shift mutation caused by a base pair insertion that results in a premature stop codon that prevents translation. (11)  

The typical pathology in the lung is alveolar proteinosis. Distended alveoli are filled with proteinaceous material and detached alveolar epithelial cells, and the alveolar septa are thickened. In the airways, SP-B is markedly reduced or absent and, by comparison, there are large amounts of abnormal SP-A and SP-C. Abnormal processing of SP-C results in its accumulation within type 2 pneumocytes. Ultrastructural examination reveals an absence of normal lamellar bodies and tubular myelin, which are replaced by multivesicular bodies and multilamellated structures. There also is an accumulation of lipid vesicles between the alveolar epithelium and its basement membrane. (12)  

To date, no human infants who lack SP-A have been identified. Abnormalities of SP-C and SP-D have been identified but do not appear to be associated with respiratory distress in human infants.  

**MAS**  
MAS is defined as respiratory distress in an infant born through meconium-stained amniotic fluid whose symptoms cannot otherwise be explained. Historically, many of these infants were postmature, although this is seen less often today because obstetricians rarely allow pregnancy to continue to more than 41 weeks’ gestation. Approximately 13% of all live births are complicated by meconium-stained amniotic fluid, and of these, 4% to 5% of infants develop MAS. (13)  

The mechanisms of injury include direct toxicity of the meconium causing chemical pneumonitis, inactivation of surfactant, activation of complement, and vasocostriction as well as partial or complete airway obstruction by the thick, particulate meconium. Secondary pulmonary hypertension is a frequent associated finding.  

The management of MAS remains a challenge. (14) Before delivery, the infusion of isotonic solution into the amniotic cavity via a catheter is termed amnioinfusion. Studies have shown that this intervention in pregnancies complicated by thick meconium and oligohydramnios can reduce the rate of MAS and fetal distress significantly. However, in view of significant adverse effects, this has not become an accepted therapy. (14)  

Current recommendations are to perform intrapartum oropharyngeal suction before delivery of the body in all cases of meconium-stained amniotic fluid. This approach recently was challenged by a large multicenter, randomized, controlled trial that included more than 2,000 infants and showed no beneficial effect of suctioning on the incidence of MAS. (15) Results of this study may influence practice significantly. Similarly, elective intubation and tracheal suction was a standard therapy in the past, although this practice also has not withstood the test of time. Wiswell and coworkers, in their large randomized study, showed no difference in the rate of MAS in neonates who were intubated and had tracheal suctioning compared with those who were not intubated. (16) Another prospective randomized study designed to determine whether routine tracheal suctioning is indicated in all meconium-stained healthy term neonates showed that the procedure was not harmless and is unnecessary in a vigorous term neonate who has meconium-stained fluid. (17)  

Because meconium is known to inactivate surfactant, exogenous replacement therapy seems logical. Randomized, controlled studies have shown that surfactant treatment reduces the need for ECMO and may reduce the risk for pneumothorax in neonates who have MAS. (18) Calf lung surfactant therapy was shown to cause significant, but short-term improvement in the oxygenation index. (19) This suggests a dose-response relationship between the surfactant inactivation and its replacement. Another method for surfactant administration in MAS is as a lavage with diluted surfactant. The use of lavage can help to remove meconium while simultaneously replacing the inactivated surfactant. (20)(21)
The use of inhaled nitric oxide (iNO) increases oxygenation in neonates who have MAS. Since the approval of iNO by the United States Food and Drug Administration in 2001, there has been a steady decrease in the use of ECMO for neonates who have MAS. (22)

Treatment of MAS has improved over the last decade with new ventilatory modalities, such as different methods of high-frequency ventilation, but no randomized trials have compared the different forms of ventilation in this setting. Experimental studies in animals have compared the use of high-frequency ventilation with conventional ventilation and have shown enhanced carbon dioxide elimination, increased lung compliance, and diminished right-to-left shunts. (14) Despite these advances, MAS remains a challenging condition with a significant mortality risk.

**Pneumonia**

Pneumonia may be acquired in utero, during delivery (or perinatally), or postnatally in the nursery or at home. It may be classified as either early-(<7 d of age) or late-onset (>7 d of age).

At autopsies of both stillbirths and liveborn neonatal deaths, pneumonia was found to be present in 20% to 60% in different centers. (23)(24) The definition of the pneumonia was based on the presence of polymorphonuclear leukocytes in the alveoli or interstitium, although the presence of bacteria was not necessary for the definition.

The causative agent varies, depending on whether the infection is acquired before, during, or after birth in the nursery or at home. (24) Intrauterine infection is usually the result of maternal infection, which may be transmitted transplacentally and involves many organs (including blood, liver, central nervous system, lungs). Pathogens include rubella, cytomegalovirus, herpes simplex virus, mumps, adenovirus, *Toxoplasma gondii*, *Treponema pallidum*, *Mycobacterium tuberculosis*, *Listeria monocytogenes*, *Varicella zoster*, and human immunodeficiency virus.

Pneumonias that are acquired at birth most often are caused by group B *Streptococcus*, but *Escherichia coli*, *Klebsiella* sp, and *Chlamydia trachomatis* also are seen. *C. trachomatis* pneumonia typically presents at a later age (3 wk). Pneumonias acquired after birth in the nursery or at home include those caused by respiratory viruses (adenovirus, respiratory syncytial virus), gram-positive bacteria (groups A, B, and G streptococci or *Staphylococcus aureus*), and gram-negative enteric bacteria (*Klebsiella* sp, *Proteus* sp, *Pseudomonas aeruginosa*, flavobacteria, *Serratia marcescens*, and *E coli*). (25)

Congenital pneumonia is a severe disease that frequently results in either stillbirth or death within the first 24 hours after birth. Pneumonias that are acquired later present most often as systemic disease. Management includes oxygen therapy, ventilatory support, antibiotics, and often vasopressor support such as dopamine and dobutamine.

**Lymphangiectasia**

Congenital errors of lymphatic development can lead to primary pulmonary disorders that include lymphangiomma, lymphangiectasia, lymphangiomatosis, and lymphatic dysplasia syndrome. (26) Because of their rarity, they often are misdiagnosed. The origins of these disorders are unknown.

Primary lymphangiectasia is a congenital disorder of the lymphatic system characterized by marked dilation of the lymphatic vessels that leads to obstruction and leakage of fluid. (27) This is seen in the visceral pleura as well as interlobular septa and results in chylothoraces, which lead to respiratory compromise or failure. Intestinal and thoracic lymphangiectasia may occur in isolation or simultaneously in the same patient as part of a generalized lymphatic dysplasia. Primary lymphangiectasia is a rare congenital malformation, with the age of presentation ranging from in utero to early adulthood. When present in the neonatal period, the clinical course is usually fatal.

The lymphatic vascular system develops during the sixth week of fetal life as an outgrowth of the venous system or as a de novo differentiation within the mesenchymal tissue. They join one another to form the lymphatic channels. The pulmonary lymphatic channels develop before the 20th week of fetal life. Primary congenital lymphangiectasia results from failure of the pulmonary interstitial connective tissue to regress, leading to dilation of pulmonary lymphatic capillaries. The lung appears heavy and noncompliant. The visceral pleura have a network of dilated lymphatics that weep lymph fluid when sectioned. Open lung biopsy is required to make the diagnosis. Supportive therapy, including albumin infusions, diuretics, thoracocentesis, and paracentesis, provide transient relief of symptoms. Dietary modifications are aimed at controlling symptoms and consequences of lymphatic obstruction but do not modify the underlying disease process. Primary pulmonary lymphangiectasia often is associated with a number of congenital and genetic diseases, including Noonan, Ullrich-Turner, Ehlers-Danlos, and Down syndromes.
Developmental Lung Abnormalities

CDH

CDH occurs in 1 in 2,000 to 4,000 births. Males are affected more often (male:female ratio of 1.5:1), and the recurrence risk in future pregnancies is 2%. CDH is a developmental abnormality of the diaphragm resulting in a defect that permits abdominal viscera to enter the chest. Usually the defect occurs before the eighth week of embryonic life. It is seen more often in the posterolateral segments of the diaphragm and more often on the left side. Some 95% occur through the posterior foramen of Bochdalek that lies posteriorly and lateral to the spine, and of these, 80% are on the left side. Classic thinking has been that the primary defect is in the diaphragm and that pulmonary hypoplasia is due to pressure from the abdominal viscera in the thoracic cavity. However, information based on the murine nitrofen-induced diaphragmatic hernia model suggests that proper formation of the diaphragm requires the normal formation of the lung and that pulmonary hypoplasia is the cause rather than the result of the diaphragmatic hernia. It has been shown that pulmonary hypoplasia occurs before the diaphragm is closed. (28) Cellular mechanisms that appear to be involved include altered regulation of expression of vascular endothelial growth factor and its receptor, fibroblast growth factors 7 and 10, insulin-like growth factor, and sonic hedgehog. Glucocorticoid receptor is increased, suggesting a protective role for glucocorticoids. Another protective factor appears to be retinoic acid. (29)

Despite the many advances in critical care and ventilator management, CDH continues to be an extremely challenging problem in the NICU. The morbidity and mortality remain high and are related primarily to pulmonary hypoplasia and pulmonary hypertension. In the delivery room, the neonate typically presents with respiratory distress shortly after birth. Physical examination may show the abdomen to be scaphoid. Air entry is reduced on the affected side, and the heart sounds are displaced. Immediate treatment includes intubation and mechanical ventilation, and a nasogastric tube should be passed for decompression. Bag-and-mask ventilation should be avoided to prevent gastric dilatation that may compromise pulmonary function further. New approaches to managing CDH that have been explored include the use of extracorporeal life support (ECMO), high-frequency ventilation, delayed surgical repair, permissive hypercapnia, nitric oxide, surfactant administration, intratracheal pulmonary ventilation, and liquid ventilation. (30) Despite the new approaches, mortality rates remain high, ranging from 25% to 74% in different reports. The presence of associated major malformations increases the mortality markedly, as does liver herniation noted at surgery. If there are no other anomalies and the defect is not part of a genetic syndrome, the prognosis after neonatal surgical repair usually is good, with overall survival rates for liveborn infants of 60% to 80%.

Congenital Cystic Adenomatoid Malformation (CCAM)

CCAM consists of a multicystic mass of dilated bronchiolar-like spaces that proliferate at the expense of alveoli. The result is the formation of a rubbery lesion that enlarges following air and fluid trapping. The cause is related to an abnormal signaling or conjugation between the developing terminal bronchioles and the alveolar mesenchyme.

Males and females are affected equally. Approximately 50% of the cases present as life-threatening respiratory distress in the neonatal period. The condition is more common on the right side, and usually only one lobe is involved. (31)

CCAM is categorized into four types. Type 1 is characterized by a small number of large cysts and is the most common (75%). In type 2, there are evenly spaced cysts that are less 1 cm in diameter. This type is associated with other congenital anomalies and poor outcome. Type 3 is rare and appears more solid on gross examination. (32) A fourth type has been defined that is characterized by acinar-type epithelium rather than the bronchiolar epithelium seen in the other three types.

At the cellular level, there is accelerated cell proliferation, with a low apoptotic index. Dysregulation of the mesenchymal growth factor, platelet-derived growth factor BB, gene expression has been implicated in the pathogenesis. (28)

Treatment is by surgical resection of the lesion. The survival rate has been reported to be 100% in neonates who do not have hydrops fetalis, but is much lower in those who have hydrops.

Congenital Lobar Emphysema (CLE)

CLE is characterized by air trapping and overdistention of segments and lobes of the lungs. It usually is diagnosed postnatally, and 50% of the cases present by the age of 6 months. Clinical symptoms include respiratory distress, mediastinal shift, and wheezing due to spontaneous overinflation of the affected areas. The upper lobes are involved in 90% of the cases. The diagnosis can be made by simple chest radiograph, but prenatal diagnosis can be made by high-resolution ultrasonography, magnetic resonance imaging, or CT. In cases that involve...
respiratory distress, the affected area should be removed. Because there are reports of spontaneous resolution, asymptomatic cases may be followed expectantly. CLE accounts for 50% of structural lesions causing respiratory distress in the newborn. It is more common in males (2:1). Sometimes the lesion can be mistaken for pneumothorax or CDH. There are associated anomalies in 14% to 40% of cases, most of which are cardiovascular. (31) (33) The prognosis is favorable, but depends on the associated abnormalities.

Pulmonary Sequestration
Lobar sequestration is composed of abnormal lung tissue that has no connection with the normal tracheobronchial tree. There are two types of lesions, and both receive their arterial blood supply from the systemic circulation, usually a branch of the aorta.

With extralobar sequestration, the discrete mass of pulmonary parenchyma is outside the pleural investment of the lung. The lesion is found on the left side, proximal to the esophagus and between the lower lobe and the diaphragm in 66% of the cases. In 80% of the cases, the blood supply derives from the descending thoracic or abdominal aorta, and the venous drainage is to the ayzygous or hemiazygous vein (80%) and the rest to the pulmonary venous system. It is more common in males (3 to 4 times), and 50% of patients have respiratory distress due to compression of the rest of the lung parenchyma. In more than 65% of cases, there are associated anomalies, including CDH (20% to 30%), pericardial defects, and total anomalous pulmonary venous return.

Abnormal expression of the homeobox gene Hoxb-5, which is necessary for normal airway branching and development, has been implicated in the etiology. (34)

Intralobar sequestration is characterized by the lesion resting within the lobe of the lung without separate pleura. It is usually in the lower lobe (95%), and in 55% of cases is on the left side. The arterial supply comes from the abdominal aorta or celiac axis, and there may be multiple feeding arteries. The venous drainage is through the pulmonary vein. Intralobar sequestration is three to six times more common than extralobar sequestration and can be an acquired lesion that results from recurrent infection. In both types, the definitive treatment is resection of the lesion. (31) (33)

Summary
Although most term infants who have respiratory distress have either TTN or infection, the differential diagnosis is extensive, and the rarer causes need to be considered in atypical circumstances.

References
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NeoReviews Quiz

9. A newborn is delivered at an estimated gestational age of 36 weeks by emergent cesarean section for fetal distress. The maternal history is significant for prolonged rupture of membranes. The infant has evidence of respiratory distress, and the chest radiograph shows patchy infiltrates and pleural effusion, as indicated by obliteration of both costophrenic angles. Of the following, the most likely cause of these chest radiographic findings in this infant is:
   A. Hyaline membrane disease.
   B. Meconium aspiration syndrome.
   C. Neonatal pneumonia.
   D. Pulmonary edema.
   E. Pulmonary hemorrhage.

10. A rare cause of respiratory distress among term newborns is a congenital abnormality of surfactant proteins. The most common of these conditions is deficiency of surfactant protein B (SP-B). Of the following, the most accurate statement regarding SP-B is that:
   A. SP-B deficiency is accompanied by reductions in SP-A and SP-C in airways.
   B. SP-B deficiency is transmitted as an autosomal dominant trait.
   C. The gene for SP-B is located on chromosome 22.
   D. The most common defect in SP-B deficiency is a frame shift mutation.
   E. The typical pathologic finding in SP-B deficiency is generalized alveolar atelectasis.

11. Several developmental abnormalities of lung structure can cause respiratory distress in the newborn. Of the following, the most common structural lesion that can cause respiratory distress in the newborn is:
   A. Congenital cystic adenomatoid malformation.
   B. Congenital lobar emphysema.
   C. Primary pulmonary lymphangiectasia.
   D. Pulmonary hypoplasia.
   E. Pulmonary sequestration.
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