Neonatal ICU chest radiographs are one of the most common pediatric radiology examinations performed. As modern medicine has advanced, the lower age limit of viability has continued to decrease. Nowadays, it is not uncommon for 23 week old infants to survive. Although there are many complications associated with prematurity, to include necrotizing enterocolitis, intracranial hemorrhage, and sepsis, the most common cause of neonatal morbidity and mortality remains lung disease. This article describes the pathology and radiographic findings of some of the most common lung disease encountered in neonates.

Transient Tachypnea of the Newborn

Transient tachypnea of the newborn (TTN), also referred to as retained fetal lung fluid, wet lung disease, or transient respiratory distress, is caused by prolonged clearance of fetal lung fluid. Fetal lung fluid is not the same as amniotic fluid; rather it represents an ultrafiltrate of the fetal plasma. Symptoms of TTN include mild to moderate respiratory distress which presents at birth but may be delayed up to 6 hours. The symptoms typically peak within 36 hours after delivery and resolve by 72 hours.

Common risk factors of TTN include precipitous deliveries and cesarean sections where it is thought that retained fluid is not fully expelled from the neonate’s lungs as would occur during a normal vaginal delivery. Normally, 35% of fetal lung fluid is cleared in the first few days prior to birth secondary to increased gene expression for an epithelial sodium (Na+) channel. The rest is cleared by labor and postnatally during crying and breathing. Other risk factors include prematurity, maternal diabetes, hydrops and other forms of hypervolemia, maternal sedation, and a history of maternal smoking.

In vivo experiments demonstrate that the poor fluid absorption may be explained by a poorly developed epithelial Na+ transport protein. In utero, the fetal lung epithelium secretes chloride (Cl⁻) and fluid. Late in gestation, the lung epithelium develops Na⁺ proteins to absorb the fetal lung fluid by responding to increased catecholamines and glucocorticoids. It is thought that infants with TTN have mature surfactant and poorly developed respiratory epithelial transport proteins, as opposed to neonatal respiratory distress syndrome (NRDS) where both surfactant pathways and Na⁺ transport proteins are deficient.

Radiographic findings of TTN often include hyperinflated lungs and retained fluid within the alveoli and interstitium, to include pleural and fissural fluid, as well as increased perihilar interstitial markings (Figs. 1 and 2). Severe cases may show alveolar opacities from the retained fluid. Radiographic findings can be similar to heart failure, although without marked cardiac silhouette enlargement. Imaging findings of TTN typically improve within 24 hours as

Figure 1. Transient tachypnea of the newborn (TTN). Portable chest radiograph reveals perihilar intstitial markings and right fissural fluid, characteristic of TTN.
the excess fetal lung fluid is either absorbed or expelled.

Treatment of TTN is typically supportive with oxygen and maintenance of body temperature. As the fluid clears, the lung parenchyma may develop a reticulonodular appearance on radiographs. The fluid typically clears superiorly to inferiorly and peripherally to centrally, although this may be variable given patient positioning.

Meconium Aspiration Syndrome

Meconium aspiration syndrome (MAS) is the most common cause of respiratory distress in the term or post-term neonate. Meconium is the earliest stool in an infant, and its components include epithelial cells, mucus, amniotic fluid, bile, blood, and lipids. Meconium was once thought to be sterile, although research has shown that approximately half of meconium is populated by Escherichia coli and the remaining half by lactic acid producing bacteria, such as Lactobacillus.3

Most cases of meconium aspiration occur during the distress of labor; however, in utero meconium passage and aspiration can occur secondary to fetal stressors, such as hypoxia and sepsis. These stressful events cause a vagal response by the fetus, leading to defecation.

Clinically, infants may present with cyanosis, tachypnea, and tachycardia. Signs of respiratory distress are invariably present, including intercostal retractions and nasal flaring. If the neonate defecated in utero, ingestion of meconium within the amniotic fluid can result in a yellow or greenish appearance to the skin, nails, and urine.

Aspiration of meconium results in airway obstruction with a ball-valve mechanism, chemical pneumonitis, and inactivation of surfactant by the bile salts, causing secondary surfactant deficiency.4 This complex pathophysiology results in a wide range of radiographic manifestations of the disease.

The most common radiographic finding is pulmonary hyperinflation secondary to the ball-valve mechanism of air trapping. Air trapping, in combination with the chemical pneumonitis, results in barotrauma which may cause pneumothoraces, pneumomediastinum, and pulmonary interstitial emphysema (Fig. 3). Other radiographic findings include perihilar ropey opacities and interspersed areas of atelectasis (Fig. 4). Pleural effusions can be seen but are uncommon.

Figure 2. Transient tachypnea of the newborn (TTN). Portable chest radiograph demonstrates perihilar interstitial markings, which can be seen with TTN from the retained fetal lung fluid.

Figure 3. Meconium aspiration. Portable chest radiograph demonstrates hyperinflation with an anteromedial pneumothorax on the right.
Meconium aspiration syndrome can result in persistent pulmonary hypertension of the newborn. Treatment includes endotracheal intubation to facilitate suctioning below the vocal cords, administration of surfactant to replace the surfactant inactivated by bile salts, and prophylactic antibiotics. The radiographic manifestations usually resolve by 48 hours, although may take weeks if the meconium has a lower water content.

Meconium aspiration results in significant morbidity and requires extensive treatment. Singh, et al. studied 7,518 neonates with the diagnosis of meconium aspiration syndrome. 9% of the patients required ICU admission, 2.4% required transfer to another NICU for convalescent care, and 1.2% died.\(^5\)

**Neonatal Respiratory Distress Syndrome**

Neonatal respiratory distress syndrome (NRDS) is the clinical term used to describe surfactant deficiency. It is also referred to as lung disease of prematurity. The term hyaline membrane disease is a histologic term and describes a byproduct of the disease.

The incidence of NRDS is approximately 6 in 1000 births.\(^6\) Risk factors include prematurity, multiple gestations, oligohydramnios, and maternal diabetes. Maternal diabetes is thought to cause fetal hyperinsulinemia which interferes with surfactant biosynthesis, leading to NRDS. Boys and Caucasian babies are also at increased risk, for unknown reasons.

Surfactant is produced in the endoplasmic reticulum of type II pneumocytes, which are found in the alveolar walls. The surfactant is transported to the surface of the pneumocyte where it is combined with surfactant apoproteins on the surface to form a lipid monolayer. The surfactant layer reduces the surface tension and allows the alveoli to more easily expand. If the type II pneumocytes are not mature at the time of birth, surfactant deficiency occurs. The collapsed alveoli result in decreased oxygenation, causing an increase in the pulmonary vascular resistance. This in turn increases right to left shunting through a patent ductus arteriosus, which usually does not close in the setting of prematurity and low blood oxygenation. The increased shunting through the PDA exacerbates the infant’s hypoxia.\(^6\)

The term hyaline membrane disease is derived from the appearance of hyaline membranes in the bronchiole walls. The hyaline membranes, which contain fibrin, mucin, and necrotic alveolar cells, are a byproduct of prolonged alveolar collapse. The lecithin to sphingomyelin ratio in the amniotic fluid is
frequently used as a marker of fetal lung maturity. Fetal lung fluid flows into the amniotic fluid throughout gestation. At approximately 32 to 33 weeks of gestational age the lecithin content rapidly increases, indicating maturing fetal lungs and production of surfactant by type II pneumocytes.

Radiographic findings in the setting of NRDS include stigmata of prematurity, to include a bell-shaped thorax and absence of humeral head ossification centers. The classic pattern of NRDS includes bilateral and symmetric granular opacities, air bronchograms, effacement of the pulmonary vasculature, and decreased lung volumes (Fig. 5). The classic appearance of NRDS is less commonly seen given the early administration of surfactant, frequently before baseline imaging is obtained, and tendency for early intubation. This results in appearances that can mimic meconium aspiration syndrome or neonatal pneumonia with increased lung volumes and focal areas of consolidation. Cystic lucencies from expanded parenchyma and asymmetric aeration can resemble PIE. If only a single lung receives surfactant, it may asymmetrically expand and cause mediastinal shift.

Dinger, et al. reported radiographic findings in 110 neonates after treatment with surfactant. Uniform improvement was shown in 38%, asymmetric improvement in 35%, and no improvement in 10%. They found that the asymmetric improvement was most pronounced in the middle and upper right lung fields.7

Symptoms, which usually present in the first hours of life, include expiratory grunting and nasal flaring with possible cyanosis. Treatment includes exogenous surfactant administration and mechanical ventilation. If these therapies are not sufficient, extracorporeal membrane oxygenation (ECMO) can be used to allow the lungs to mature. Complications include barotrauma from mechanical ventilation and oxygen toxicity of the pulmonary parenchyma, as well as hemorrhage from surfactant therapy.

**Bronchopulmonary Dysplasia**

Bronchopulmonary dysplasia (BPD), also known as chronic lung disease of infancy, is a disease of unclear etiology, although it is likely multifactorial. The disease was originally thought to be caused from NRDS and its treatment. The etiology of BPD is now less clear given the advancements in neonatal treatment for NRDS, such as surfactant, steroids, and low pressure algorithms of positive pressure ventilation. Infectious organisms, such as *Ureaplasma urealyticum*, which is the most common contaminant in amniotic fluid, have also been implicated as potential causes of BPD. It has been postulated that inflammatory cytokines associated with *Ureaplasma* infection injures the respiratory epithelium, which is then further damaged by oxygen toxicity or barotrauma.6,8,9

The radiographic findings of BPD vary and have evolved over time from continuing advances in medical therapy. Northway, et al. originally described four radiographic stages of BPD: stage 1 (2-3 days after birth) resulted in the typically granular opacities of NRDS; stage 2 (4-10 days) demonstrated granular opacities and with superimposed complete pulmonary opacification in more severe cases (Fig. 6); stage 3 (10-30 days) revealed small cystic lucencies alternating with small focal opacities; and stage 4 (greater than one month) showing a “bubbly” appearance due to enlargement of cystic lucencies and linear or ropy opacities.10

![Figure 6. Bronchopulomonary dysplasia (BPD).](image)

Portable chest radiograph of a neonate with bronchopulmonary dysplasia demonstrates diffuse granular opacities with more focal consolidation in the right lung.
Interstitial gas may extend along numerous potential spaces in the interstitium toward the peripheral lung. Subpleural blebs can form and rupture, resulting in a pneumothorax. Interstitial gas may also extend centrally, resulting in pneumomediastinum. The radiographic appearance of PIE can occasionally be confused with aspiration pneumonia, pulmonary edema, and neonatal respiratory distress syndrome.¹²

There are two types of PIE, acute and persistent. Acute PIE appears radiographically as “bizarre tubular and cystic lucencies” which may be focal or diffuse (Fig. 7). The term persistent PIE is reserved for PIE that lasts longer than 1 week. As with the acute form, it may be focal or diffuse. The cysts of persistent PIE have been described as being lined with multinucleated giant cells.⁶ Persistent PIE may be confused with other types of cystic thoracic chest masses in the infant. However, PIE can usually be distinguished from other cystic lesions, since it arises occurs and progresses in a ventilated patient.

Management of PIE varies and includes high-frequency ventilation, placing the affected side of the chest down if the PIE is unilateral, and selective bronchial intubation to help spare the affected lung. Persistent PIE is managed conservatively, although focal cases can be resected if they are severe. If successfully treated, radiographic findings improve or resolve, depending upon the degree of improvement and underlying parenchymal injuries (Fig. 8).

Summary

Neonatal lung disease remains one of the most common causes of morbidity and mortality in this patient population, especially in the setting of prematurity. Neonatal chest radiographs play a critical role in the diagnosis, categorization, and management of the myriad of underlying neonatal lung diseases. Therefore, it is critical that radiologists involved in interpreting neonatal chest radiographs be familiar with the imaging manifestations of common neonatal lung pathologies. This will allow for prompt and accurate characterization, as well as expedite and guide treatment.

Swischuck, et al. studied the effects of surfactant and oxygen therapy on the radiographic evolution of NRDS. 75 premature infants were studied and 45% demonstrated prompt clearing of the granular opacities. 31% demonstrated transitioning of the granular opacities into a hazy lung opacity, of which 35% subsequently cleared and 65% progressed to the bubbly lung appearance of BPD. They reported that younger and smaller infants were more likely to progress to BPD.¹¹

There is significant morbidity associated with BPD secondary to increased incidence of reactive airway disease, infection, and pulmonary artery hypertension, which can result in cor pulmonale when severe. Current treatment is largely supportive with oxygen therapy and prompt treatment of pulmonary infection.

**Interstitial Air**

The use of mechanical ventilation exposes the lungs to increased pressure, termed barotrauma, and over distention, called volutrauma, resulting in lung injury. Injury resulting in rupture at the junction of terminal bronchioles and alveoli, which allows gas to infiltrate into the perivascular and peribronchial spaces. This is referred to as pulmonary interstitial emphysema or PIE.
Figure 8. Development and resolution of PIE.
Portable chest radiograph in a premature newborn infant (A) demonstrates an endotracheal tube tip near the carina, diffuse granular opacities, and no interstitial air. Examination performed two days later (B) shows interval development of PIE within the left pulmonary interstitium. Three days later, the right lung develops PIE (C). By two weeks from the initial radiograph, the pulmonary interstitial emphysema has resolved (D).

References

