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Respiratory Disorders of the Foal: Neonate Onward

Pamela A. Wilkins, DVM, MS, PhD, Diplomate ACVIM, Diplomate ACVECC

Author’s address: University of Pennsylvania School of Veterinary Medicine, New Bolton Center, 382 West Street Road, Kennett Square, PA 19382; Email: pwilkins@vet.upenn.edu.

Take Home Message

There are a variety of conditions that can affect the foal in the first year of life from birth forward. Respiratory problems are relatively common in this age group and the respiratory tract should be examined thoroughly in any ill foal.

Early recognition of abnormalities in the respiratory tract is of utmost importance for the successful management of ill foals. In order to recognize abnormal, the normal must be known. Immediately following birth, foals effect several important physiological and behavioral changes. Chief amongst these changes are the adaptation of the cardiovascular and respiratory systems to extraterrestrial life. The normal transition of the respiratory tract involves opening closed alveoli and absorption of fluid from the airway, accomplished by a combination of breathing efforts, expiration against a closed glottis (‘grunting’) and a change in sodium flux across the respiratory membrane from net secretion to net absorption. The transition from fetal to neonatal circulatory patterns requires resolution of the pulmonary hypertension present in the fetus, normally shunting blood flow through the lower resistance ductus arteriosus in the fetal state, in order to direct cardiac output to the pulmonary vasculature for participation in gas exchange. This change is achieved by the opening of alveoli, decreasing airway resistance and providing radial support for pulmonary vessels, functional closure of the ductus arteriosus and also by increasing the oxygen tension in the lung, reversing pulmonary vasoconstriction mediated by hypoxia. In the normal newborn this change is smooth and rapid. These critical events are undermined by factors such as inadequate lung development, surfactant deficiency (primary or secondary), viral or bacterial infection, placental abnormalities, in utero hypoxia and meconium aspiration.

Spontaneous breathing should begin in the neonate within 1 minute of birth, many foals will be attempting to breathe as their thorax clears the pelvic canal. During the first hour of life, the respiratory rate of a healthy foal can be as high as 80 breaths per minute, but should decrease to 30-40 breaths per minute within a few hours. Similarly, the heart rate of a healthy newborn foal will have a regular rhythm and be at least 60 beats per minute at the first minute.

Auscultation of the thorax shortly after birth will reveal a cacophony of sounds as airways are opened and fluid is cleared. End-expiratory crackles are consistently heard in the dependent lung during and following lateral recumbency. It is not unusual for a normal newborn foal to appear slightly cyanotic during this initial adaptation period but this should resolve within minutes of birth. The equine fetus, as do all feti, exists in a moderately hypoxic environment, but the equine fetus has a greater partial pressure of oxygen, around 50 mmHg. Because the fetus is well adapted to low oxygen tensions, cyanosis is rarely present in newborn foals once adaption
occurs, even those with low oxygen tensions. The presence of significant cyanosis that persists should prompt the clinician to thoroughly evaluate the foal for cardiac anomalies resulting in significant right to left shunting or separated circulations, such as transposition of the great vessels.

The chest wall of the foal is very compliant, facilitating passage through the pelvic canal during parturition. This compliance requires that the foal actively participate in both inspiration and expiration with several potential consequences. First, restriction of the thorax or the abdomen can result in impaired ventilation. This can easily occur when restraining a foal and may result in spuriously abnormal arterial blood gas values. Second, foals with primary pulmonary parenchymal disease resulting in poorly compliant lungs will develop paradoxical chest wall motion, with the thorax moving inward during inspiration.12-15 The work of breathing can be greatly increased, resulting in respiratory failure due to respiratory muscle fatigue. A foal that appears to suddenly improve a previously abnormal respiratory rate and pattern may in fact be in greater respiratory difficulty due to fatigue. A reduction in respiratory rate or abnormal breathing pattern can be observed in premature/dysmature foals or foals subjected to peripartum hypoxia/asphyxia. Foals attempting to maintain an adequate lung volume will expire against a partially closed glottis, called the “Valsalva maneuver”, producing an audible “grunt”.

**Persistent Pulmonary Hypertension of the Newborn**

Persistent Pulmonary Hypertension (PPH) is also known as reversion to fetal circulation or persistent fetal circulation and its genesis lies in the failure of the fetus to successfully make the respiratory and cardiac transition to extra-uterine life or reversion of the newborn to fetal circulatory patterns in response to hypoxia and/or acidosis. Differentiating this problem from other causes of hypoxemia in the newborn, such as sepsis or bacterial or viral pneumonia, or congenital cardiac malformation, requires some investigation and multiple serial arterial blood gas analyses are necessary to confirm suspicion of this problem. However, the condition should be suspected in any neonate with hypercapnic hypoxemia that persists and worsens; these foals are in hypoxemic respiratory failure. The fetal circulatory pattern, with pulmonary hypertension and right to left shunting of blood through the patent foramen ovale and ductus arteriosus is maintained in these cases.

Pulmonary vascular resistance falls at delivery to ~10% of fetal values while pulmonary blood flow increases accordingly.16 Early in the postnatal period these two changes balance each other out and mean and systolic pulmonary pressures remain increased for several hours. The direct effects of lung expansion and increasing alveolar oxygen tension probably provide the initial stimulus for pulmonary arteriolar dilation. Partly this is due to direct physical effects, but vasoactive substances are released in response to physical forces associated with ventilation, for example protacyclin.16 The increase in alveolar and arterial oxygen tensions at birth is required for completion of resolution of pulmonary hypertension. It is thought that much of this is mediated by NO, evidence for this being the parallel increase during gestation of the pulmonary vasodilation response to hyperoxia and the increase in NO synthesis.17 However, inhibition of NO synthesis does not eliminate the initial decrease in pulmonary artery resistance occurring due to opening of the airways.18
It is when these mechanisms fail that PPH is recognized. Right to left shunting within the lungs and through patent fetal conduits occurs. This can be secondary to many factors, including asphyxia and meconium aspiration, but in many cases the precipitating trigger is unknown. Treatment of PPH is two-pronged: abolishment of hypoxia and correction of the acidosis, as both abnormalities only bolster the fetal circulatory pattern. Initial therapy is provision of intranasal oxygen (INO₂) at 8-10 L/min. Some foals will respond to this therapy and establish neonatal circulatory patterns within a few hours. Failure to improve, or worsening of, hypoxemic respiratory failure following INO₂ should prompt intubation and mechanical ventilation with 100% oxygen. This serves two purposes, one diagnostic and one therapeutic. Ventilation with 100% O₂ may resolve PPH and, if intrapulmonary shunt and altered ventilation perfusion relationships are causing the hypoxic respiratory failure arterial oxygen tension (PaO₂) should exceed 100 mmHg under these conditions. Failure to improve PaO₂ suggests PPH or large right to left extrapulmonary shunt due to congenital cardiac anomaly. The vasodilators prostacyclin and tolazoline (an α-blocking vasodilator) will cause pulmonary vasodilation in human infants with PPH, but the effects on oxygenation are variable and the side-effects (tachycardia, severe systemic hypotension) are unacceptable. Recognition of NO as a potent dilator of pulmonary vessels has created a significant step forward in the treatment of these patients, as inhaled NO dilates vessels in ventilated portions of the lung while having minimal effects on the systemic circulation. Based on evidence presently available, it appears reasonable to use inhaled nitric oxide in an initial concentration of ~20 ppm in the ventilatory gas for term and near term foals with hypoxic respiratory failure and PPH that fails to respond to mechanical ventilation using 100% oxygen alone. We have used this approach in our clinic, administering a range of 5-40 ppm NO, with success. We have also investigated the use of sildenafil, 20 mg PO Q4-6 hours, as pulmonary vasodilator in some of these cases to good effect in a few.

Meconium Aspiration Syndrome (MAS):

Meconium aspiration is thought to occur secondary to acute pre- or intrapartum asphyxia associated with severe fetal distress, subsequent passage of meconium by the fetus and aspiration of meconium during fetal gasping efforts. Neonates with meconium aspiration syndrome (MAS) have marked surfactant dysfunction. Airways and alveoli of affected neonates contain meconium, inflammatory cells, inflammatory mediators, edema fluid, protein, and other debris. Meconium aspiration syndrome can present clinically with different degrees of severity, ranging from a mild form of respiratory compromise to severe forms that may result in perinatal death despite respiratory management up to and including mechanical ventilation and extracorporeal membrane oxygenation (ECMO). However, advances in our knowledge concerning meconium aspiration syndrome have revealed that many cases of severe meconium aspiration syndrome in humans may not be causally related to the aspiration of meconium but rather are caused by other pathologic processes occurring in utero, primarily chronic asphyxia and infection. Current treatments being investigated in the management of human infants with MAS include surfactant administration, surfactant administration combined with partial liquid ventilation and surfactant lavage.

Bacterial Pneumonia:
In the neonate, bacterial pneumonia is usually secondary to sepsis or aspiration during suckling. Foals with sepsis can also develop acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) as part of the systemic response to sepsis and this is frequently a contributor to the demise of foals in septic shock. Diagnosis of bacterial pneumonia is supported by transtracheal aspirate culture and cytology, but blood culture can aid in early identification of the causative organism and allow for early institution of directed antimicrobial therapy. Radiography and thoracic ultrasonography are useful additional diagnostic aids. Auscultation and percussion of the thorax should be performed and any noted abnormalities addressed; however, thoracic auscultation can be surprisingly unremarkable in some foals with significant pulmonary disease. The isolated organisms from this type of bacterial pneumonia of the neonate reflect those commonly isolated in sepsis in newborns: *E. coli*, *Klebsiella* spp, *Actinobacillus equuli*, etc. Initial antimicrobial treatment should be a broad-spectrum bactericidal combination, such as penicillin and amikacin. Antimicrobial therapy can then be altered based on culture and sensitivity patterns of the isolated pathogens. Serial white blood cell counts, differentials and determinations of plasma fibrinogen concentration are useful for monitoring response to therapy. The distribution of bacterial pneumonia secondary to sepsis tends to be generalized throughout the lung.

A second frequent cause of bacterial pneumonia in the neonate is aspiration due to poor suck reflex or dysphagia associated with perinatal asphyxia syndrome (PAS), sepsis or weakness. Multiple organisms may be isolated from transtracheal aspirates with this form of pneumonia. The distribution tends to be cranioventral. Care must be taken to ensure that aspiration is not iatrogenic in foals being bottle-fed. Foals being bottle-fed or fed via nasoesophageal tubes should be in sternal recumbency or standing and remain so for at least 10 minutes once feeding is complete to prevent passive esophageal regurgitation following changes in position of the head and neck. Some foals with neonatal encephalopathy and poor suck reflexes will not protect their airway well and will aspirate their own saliva, even when not allowed to suck from their dam or a bottle. Auscultation over the trachea while the foal is sucking will help identify occult aspiration in suckling foals. Occult aspiration pneumonia should be suspected in any critically ill neonate that is being bottle-fed, or is suckling on its own, that has unexplained fever, fails to gain weight or has a persistently increased fibrinogen concentration.

Older foals develop bacterial pneumonia, frequently secondary to an earlier viral infection. Auscultation and percussion of the thorax should be performed, but the results may not closely correlate with the severity of the disease. The most commonly isolated bacterial organism in this primary foal pneumonia is *Streptococcus equi var zooepidemicus* and it may be isolated alone or as a component of a mixed infection. Transtracheal aspirate for culture and cytology is recommended as mixed Gram positive and Gram negative infections are common and antimicrobial susceptibility patterns can be unpredictable. The obtained aspirate should be split and submitted for bacterial culture, virus isolation and cytology. Additional diagnostics include radiography, ultrasonography and serial determination of white blood cell counts (with differential) and blood fibrinogen concentrations. Treatment is by administration of appropriate antimicrobial therapy. Some foals may benefit from nebulization with saline or other local products. Ascarid larval migration through the lung can mimic bacterial pneumonia. In these cases, the foal may not respond to antimicrobial therapy and should be dewormed with...
ivermectins. Deworming of the mare within 1 month of parturition and frequent deworming of the foal will prevent ascarid migration pneumonia in most cases.

Viral Pneumonia

The most commonly identified causes of viral pneumonia in foals are equine herpes viruses 1 and 4 (EHV 1 and 4), equine influenza and equine arteritis virus (EVA). EHV 1 is probably the most clinically important, but outbreaks of EVA in neonates have occurred and are devastating.32-38 Adenovirus is reported sporadically and as a problem in Arabian foals with SCID.39-41

In the neonate, infection with EHV-1 or EVA is almost uniformly fatal and ante-mortem diagnosis is difficult, even once an outbreak on a particular farm is identified. Several factors appear common to foals with EHV-1, including icterus, leukopenia, neutropenia and petechial hemorrhage, but these problems are also identified in foals with severe sepsis.42-44 The antiviral drug acyclovir (10-16 mg/kg orally or per rectum 4-5 times per day) has been used in cases of EHV-1 in neonates, with some evidence of efficacy in mildly affected foals or foals affected after birth.44 If viral pneumonia is a possibility, blood and tracheal aspirates should be collected at presentation for bacterial and virus isolation. Mechanical ventilation of these cases may prolong life, but death is generally inevitable due to the magnitude of damage to the lung. Foals suspected of having either EHV-1 or EVA should be isolated as they are generally shedding virus and pose a threat to other neonates and any pregnant mares. Neonates born with or infected immediately post-natally with EHV-1 have a grave prognosis, although some reports exist of foals surviving this disease. Foals with neonatal EVA are generally born to seronegative mares and treatment with intravenous plasma with a high titer against EVA may prove beneficial, as passive immunity appears to have a large role in protection against this disease in neonates.38,45

Other Causes of Respiratory Signs in Foals

Rib fractures have been recognized in 3-5% of all neonatal foals and can be associated with respiratory distress.50-54 Potential complications of rib fractures include fatal myocardial puncture, hemothorax and pneumothorax. Rib fractures are frequently found during physical examination by palpation of the ribs or by auscultation over the fracture sites. Diagnosis can be confirmed by radiographic and ultrasonographic evaluation. Usually multiple ribs are affected on one side of the chest. Specific treatment is generally unnecessary, but direct pressure on the thorax should be avoided in all cases. Some specific patients may benefit from surgical stabilization of some fractures, particularly those fractures overlying the heart.51,54
Pneumothorax can occur spontaneously or secondary to excessive positive pressure ventilation. It can also occur secondary to tracheostomy surgery or trauma. Any foal being mechanically ventilated that suddenly presents respiratory distress and hypoxemia should be evaluated for pneumothorax. Diagnosis is by auscultation and percussion of the thorax, but can be confirmed with radiographic and ultrasonographic evaluation of the thorax. Needle aspiration of air from the pleural space also confirms the diagnosis. Treatment is required in cases where clinical signs are moderate to severe and/or progressive and involves closed suction of the pleural space. Subcutaneous emphysema can complicate treatment of this problem.

Idiopathic or transient tachypnea has been observed in Clydesdale, Thoroughbred and Arabian breed foals primarily. In human infants, transient tachypnea can be related to delayed absorption of fluid from the lung, perhaps due to immature sodium channels. In foals, it is generally seen when environmental conditions are warm and humid and is thought to result from immature or dysfunctional thermoregulatory mechanisms. Clinical signs are primarily increased respiratory rate and rectal temperature. Signs develop within a few days of birth and may persist for several weeks. Treatment involves moving the foal to a cooler environment, body clipping and provision of cool water or alcohol baths. These foals are frequently treated with broad-spectrum antimicrobial drugs until infectious pneumonia can be ruled out.

Bronchointerstitial pneumonia and acute respiratory distress have been described in older foals and appear to be distinct entities from acute respiratory distress syndrome seen in neonatal foals in association with sepsis. The underlying etiology has not been identified, but the genesis is probably multifactorial with several potential pathogens having roles. Affected foals present with acute respiratory distress with marked tachypnea, dyspnea, nostril flare and increased inspiratory and expiratory effort. Auscultation reveals a cacophony of abnormal sounds including crackles and polyphonic wheezes in all lung fields. Loud bronchial sounds are heard over central airways and bronchovesicular sounds are lost peripherally. Affected foals are cyanotic, febrile and unwilling to move or eat. Foals may be found acutely dead. Laboratory abnormalities include leukocytosis, hyperfibrinogenemia and hypoxemia with hypercapnic acidosis. Foals can be severely dehydrated and have coagulation changes consistent with disseminated intravascular coagulation. Hypoxic injury to other organs, primarily kidney and liver, can be recognized. Chest radiographs reveal a prominent interstitial pattern overlying a broncho-alveolar pattern that is diffusely distributed throughout the lung. This syndrome is a respiratory emergency. Treatment is broad-based and includes administration of oxygen, non-steroidal anti-inflammatory agents, broad-spectrum antimicrobial therapy, nebulization, judicious intravenous fluid therapy, nutritional support and corticosteroid therapy. Hyperthermia needs to be managed. Corticosteroid therapy appears to have been life-saving in most of the reported surviving foals. Because this syndrome is associated with high environmental temperatures in some areas, prevention involves control of ambient temperatures, not transporting foals during hot weather and keeping foals out direct sun on hot days, particularly foals being treated with erythromycin for suspected or confirmed R. equi infection.

References


