

Medical Issues for the Neonatal Foal: Prematurity and Sepsis

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Prematurity

A variety of maternal illnesses may result in premature delivery of a foal. Placentitis remains the most common disorder responsible for delivery of premature foals in our practice. The most important issue for the premature foal is “readiness-for-birth.” Rossdale’s group has provided our profession with significant advances in our understanding of the concept of “readiness-for-birth. (that being a well-developed, hormonally mature foal capable of extrauterine survival). A precise definition of prematurity is somewhat elusive, but a gestational age of < 320 days is considered by most authors as “premature.” Foals that have an “adequate” gestational age but “inadequate” development have been termed “immature” or “dysmature.” Further evaluation may lead to the terminology of “small for gestational age (SGA)” and “*in utero* growth retardation (IUGR).” SGA seems to be differentiated from IUGR in that neonates with SGA are normally and proportionately developed, yet have small stature compared to expected (statistical) measurements, whereas, neonates with IUGR demonstrate abnormal proportional growth patterns such as an enlarged (sometimes domed) head compared to the truncal and musculoskeletal growth.

The most commonly described clinical signs with prematurity include the following: weakness, smaller size, thin skin and hair coat, floppy ears, and flexor tendon laxity (resulting in hyperextension). Clinical laboratory data that are supportive of prematurity include: leukopenia (total WBC count $\leq 2,000$ cells/ μ L) with a reversed neutrophil:lymphocyte ratio (both suggesting adrenocortical insufficiency), and in some cases, decreased intestinal absorption of immunoglobulin. Many of these foals will have signs of respiratory system compromise; hypoventilation as seen in the clinical character of respirations, and evidence of hypoxemia ($\text{PaO}_2 < 80$ mm Hg) and hypercarbia ($\text{PaCO}_2 > 50$ mm Hg). This eventually leads to respiratory failure and subsequent multiple organ failure as a consequence of prolonged hypoxemia.

There are some foals that appear to be in a “transitional” state between prematurity and “ready-for-birth” and are described as “twilight” foals. They may be leukopenic at birth, but rapidly switch to a normal or even elevated WBC count with an appropriate or regenerative differential count.

In the case of many premature foals as well as those in the IUGR category, incomplete ossification of the cuboidal bones may be a significant issue. The only certain way to determine this is by radiography of the tarsus and carpus to determine the extent of ossification. References are available for grading the degree of ossification.

Survival of the premature foal remains poor, even with significant efforts in the intensive care unit. Even with extensive support including hormonal stimulation (corticosteroids), respiratory support (surfactant, mechanical ventilation with inhalant therapy in some cases), and general intensive care support, the survival rate of foals less than 310 days is poor. In some performance-oriented breeds, practicality is more of an issue and most of these foals are euthanized early on due to poor prognosis for athletic ability. Unfortunately, advances in the treatment of prematurity remain slow due to the low number of patients in which medical care is attempted. Each patient becomes a clinical trial with an “n” of 1.

In foals that are considered in the “twilight” stage or possibly IUGR, hormonal supplementation is sometimes helpful. A precise dose regimen is not known, but the author frequently uses methylprednisolone sodium succinate (Solu-Delta-Cortef[®] – 100 mg/50 kg foal, IV, q 12 or q 6 hours). Supplemental growth hormone may also be beneficial for supporting musculoskeletal growth and possibly a neuroprotective effect for birth asphyxia (EquiGen[®] – 2.5 mg IM, SID, BresaGen).

Birth asphyxia remains an important issue for foals born from placental abnormalities. Neuroprotection is the newest area of medical advance for birth asphyxia. This topic is being covered in a separate presentation (Immediate Care of the Compromised Foal).

Sepsis

Sepsis remains an important source of clinical illness for the neonate and older foal. As we are all aware, hypogammaglobulinemia secondary to failure of passive transfer of colostral antibodies is an important predisposing factor. Yet, we still see sepsis in foals with adequate plasma IgG concentrations, so other poorly defined risk factors remain. The routes of infection commonly listed include: oral-gastrointestinal, respiratory, transcutaneous, and umbilical. With the recognition and precautionary disinfection of the umbilical stalk being a common practice, this route seems much less common today compared with the gastrointestinal or other routes. Early recognition of bacterial sepsis is still difficult as sick foals with a variety of medical issues (birth asphyxia, hypoglycemia, etc.) may appear similar (weak, somnolent, recumbent) to those with sepsis. Leukopenia is the most important laboratory finding in sepsis, yet it is not specific to bacterial infection as it can occur with prematurity, neonatal herpes virus infection, and alloimmune neutropenia (associated with binding of colostral antibodies to circulating neutrophils resulting their removal by the reticuloendothelial system). This can confound the evaluation of an affected foal for the presence of sepsis – affected foals are often clinically normal, but maintain low WBC counts for many days. The blood smear can be an important source of information as the presence of a left shift as well as toxic changes in the neutrophils are findings that are supportive of sepsis. Blood culture prior to administration of antibiotics is still the most important diagnostic test. In some cases this can provide critical information in antibiotic selection in some patients.

In spite of appropriate antibiotic therapy, many neonates with sepsis will die. This is the same as occurs in other species, including humans. In the last couple of decades, the

inflammatory mediator cascade has been thoroughly described, leading to the definition of “systemic inflammatory response syndrome” or “SIRS.”¹ It is now known that SIRS is often the final common denominator leading to multiple organ failure in septic patients. Treatment (or preferably prevention) of the effects of the inflammatory cascade and the subsequent multiple organ dysfunction or failure is now known to be as (or more) important than the antibiotic therapy for sepsis. There have been many studies demonstrating the presence of the same inflammatory mediators (IL-1, TNF- α , platelet activating factor, prostaglandins, etc) in foals with sepsis as well as many studies evaluating blockade of these specific mediators. The basic point is that there is such overlap and redundancy of mediators, that no single “silver bullet” is available (nor likely to be found).

Once sepsis has been recognized (or more commonly highly suspected), appropriate treatment is necessary to improve the outcome beyond antibiotics alone. Commonly available medications that may be effective in blocking certain inflammatory mediators include:

Banamine^r – flunixin meglumine – cyclo-oxygenase type I and II inhibition

Polymixin B – binds lipopolysaccharide component of endotoxin and prevents its binding to monocyte membrane receptors

Pentoxifylline – phosphodiesterase inhibitor – prevents release of IL-1 and TNF- α from monocytes

Corticosteroids – the use of these in sepsis has cycled over the years, but there is some recent evidence that these may reduce circulating mediator levels and thus be useful in preventing or reducing the effects of the inflammatory response.

It is important to understand that these medications are most effective when administered prior to exposure to endotoxin. This may have some practical use in that it is possibly beneficial to pretreat a foal that is suspected of being septic with one or more of these medications prior to administering the antibiotics.

Certainly, attention to the level of plasma immunoglobulin is important in sepsis for the opsonizing effects, but it is also important to remember that there may be certain anti-inflammatory benefits from plasma components as well.

Fluid therapy and supportive care still make the difference in the outcome for foals that show signs of hypotension or septic shock. Crystalloid fluids (balanced electrolytes) are the mainstay of fluid resuscitation. Hypoglycemia is common in weak foals showing signs of sepsis and 50% dextrose may be added to the crystalloid fluid (50 ml of 50% dextrose added to one liter of fluids (most commonly balanced electrolyte solutions such as Normosol-R are used) makes an approximate solution of 2.5% dextrose). In certain patients, advanced stages of shock and circulatory dysfunction may require additional fluid support such as the addition of a colloid (hetastarch – 2 to 10 ml/kg as a slow

infusion) or even hypertonic saline (2 to 4 ml/kg infusion) to improve the effective circulating fluid volume.

Antimicrobial selection is still an important issue. The initial choice can often be the deciding factor in the patient's outcome. Economics often play a factor in the decision, but the best rule is to select a broad-spectrum combination to cover the many possible organisms, especially gram-negatives. Common first choices might include: penicillin plus an aminoglycoside, high-dose ceftiofur alone or in combination with another antibiotic, or advanced antimicrobial agents (if severe sepsis is already present and the economics allow for such a selection). Some of the advanced (3rd generation) cephalosporins (ceftazidime - Fortaz[®]) or imipenem-cilastatin (Primaxin[®]) may be appropriate given an understanding of common regional or nosocomial pathogens.

Nosocomial infections should be given consideration in any high-traffic facility, whether it is a hospital or high-volume farm facility. Recognition of this as an infection source, and institution of appropriate control and sanitation measures are critical for controlling nosocomial infections. There have been numerous publications describing nosocomial infections in a variety of veterinary hospitals (university and private practices), and these should now be considered a "fact of life" for the profession and should receive greater attention in the form of monitoring and prevention programs.

References:

Divers, TJ, Shock and Systemic Inflammatory Response Syndrome in *Manual of Equine Emergencies: Treatment and Procedures*, 2nd Edition, pp. 615-620.