

WHAT TO DO WITH THE SEPTIC FOAL

L. Chris Sanchez, DVM, PhD, DACVIM
College of Veterinary Medicine
University of Florida, Gainesville, FL, USA
Proceedings: North American Veterinary Conference, Orlando, FL, January 2012
Reprinted with Permission

PHYSICAL EXAMINATION FINDINGS

When examining a sick neonatal foal, think sepsis until proven otherwise! It is the leading cause of morbidity and mortality in this population, thus should never be far from your mind. Initial clinical signs can be vague and vary widely but frequently include depression, decreased or absent suckling, and lethargy, which may progress to recumbency. Dehydration becomes a more significant problem as time progresses; tachycardia and tachypnea are common. The mucous membranes often develop a bright or injected appearance and the capillary refill time may be rapid. Rectal temperature may be normal or mildly increased. Hypothermia can be associated with advanced sepsis or moderate to severe prematurity. Diarrhea is common in foals with sepsis (and no other evidence of enteric pathogens) and can be the primary presenting complaint. Other localizing signs include uveitis, seizures, joint effusion, lameness, respiratory disease or distress, subcutaneous abscesses, patent urachus, and omphalitis. It is important to note that many foals with umbilical remnant infection and/or abscessation often have normal external umbilical structures. Thus, ultrasonographic examination is recommended in any presumed septic foal.

CLINICOPATHOLOGIC FINDINGS

Leukopenia, characterized by neutropenia, is the most common hematological finding associated with acute sepsis. Premature or dysmature foals will also commonly have a decreased neutrophil count in the absence of sepsis. But, septic foals typically have a degenerative left shift with toxicity, whereas these findings are not typical of uncomplicated prematurity. In older septic foals (8-14 days), neutrophilia can be more common. A high fibrinogen concentration shortly after birth is consistent with *in-utero* infection. Hypoglycemia is common initially, especially in foals less than 24 hours of age, as are azotemia, hyperbilirubinemia, acidemia and hyperlactemia. The coagulation and fibrinolytic systems of the septic newborn are often abnormal, with clinically relevant decreases in antithrombin III and elevations in prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen, fibrin degradation products and D-dimer concentrations.

DEFINITIVE DIAGNOSIS

Blood culture is the gold standard for diagnosis of bacteremia. Identification of a causative organism allows for directed antimicrobial therapy as well as determination of patterns in infection, but is rarely practical in the field. If performed, samples should be collected from a large vein (jugular, cephalic, saphenous) after surgical clip and aseptic preparation into a sterile syringe without anticoagulant and immediately placed into blood culture media. Sterile sample collection from a venous catheter at the time of placement is also acceptable. For those foals receiving antimicrobial therapy prior to sample collection, use of a medium with resins may improve microbial recovery. For any medium, care should be taken to infuse the recommended volume of blood to promote optimum recovery.

Two main factors limit the practical usefulness of blood cultures. First, positive results are usually not available for at least 48 hours following submission. Second, a positive blood culture, while extremely specific, is not very sensitive. Thus, the modified "sepsis score" is often used to identify at risk foals. Accuracy of these systems has regional and institutional variability.^{2,3} Thus, while a "positive" score is supportive of sepsis in a suspected animal, a "negative" score alone should not be used to withhold antibiotic therapy from an at risk foal. Similarly, the use of a positive score alone, without complimentary culture results or necropsy findings, should be used cautiously to confirm a diagnosis of sepsis for retrospective studies.

CAUSATIVE ORGANISMS

Several retrospective studies have evaluated the most common organisms isolated from both blood culture and necropsy specimens in septic foals over the years. Whereas gram-positive organisms predominated in the 1940's-1950, *E. coli* has remained the predominant organism isolated from septic foals regardless of clinic location or methodology since that time. Era and geographic location appear to play a major role in prevalence of other causative organisms. In the late 1990s, gram positive bacteria (*Enterococcus*, *Streptococcus*, *Staphylococcus* spp.) cumulatively played a major role in disease pathogenesis in

Pennsylvania, whereas *Actinobacillus* spp. accounted for approximately 30% of all isolates in Ohio.^{5,6} Recently, gram positive organisms were isolated from 40.3% of all blood cultures from neonatal foals in Australia.⁶ A Florida study documented a decrease in gram-negative enteric organisms in the 2000s relative to the 1980s.⁹ Systemic fungal infections can also occur. Clinical signs include persistent fever and thrush (white plaques on the tongue). The most commonly implicated organism is *Candida albicans*. Risk factors include prolonged hospitalization and immunodeficiency.

TREATMENT

Antimicrobial therapy

Antibiotics provide the basis of therapy for septic foals. Initially a broad-spectrum bactericidal approach must be used based on previous experiences and costs. Antimicrobial therapy should begin immediately in any foal in which sepsis is suspected and should not be delayed for referral. In human ICUs, institution of antimicrobial therapy should occur within an hour of admission. Therapy can be altered if necessary when sensitivity data become available. A minimum therapeutic course of two weeks is recommended for bacteremic foals without localizing clinical signs. If localizing signs are present, a minimum course of 4 weeks is recommended.

Few published veterinary reports discuss antimicrobial sensitivity of organisms isolated from septic foals. A theme of most reports is a cumulative sensitivity of >90% of all isolates to amikacin, with a somewhat lower sensitivity to gentamicin and ceftiofur.^{7,9,10} Sensitivity clearly varies by class of organism.

Thus, based on available data, a recommended initial therapeutic approach involves combining amikacin or a third-generation cephalosporin with penicillin, ampicillin, or ceftiofur. The use of amikacin should be tempered in light of the foal's cardiovascular and renal status. If a foal is severely hypovolemic and azotemic, a safer initial choice would likely involve a cephalosporin, such as ceftiofur, alone. Therapeutic drug monitoring has been recommended to ensure appropriate dosing for aminoglycoside use. Practically, monitoring should include serial creatinine concentration measurement every 3-5 days and/or serial urinalyses including sediment examination in order to evaluate for potential renal side-effects.

Unfortunately, the range of oral antibiotics is limited in foals. Trimethoprim/sulfa combinations are not recommended as an initial therapy for septic foals, as a bacteriocidal alternative is preferable. Fluoroquinolones, such as enrofloxacin, have an excellent spectrum of activity against gram-negative and some gram-positive organisms but have been associated with arthropathy in foals. Thus, use of this agent should be reserved for those cases with documented resistance to other antimicrobial agents and informed owner consent.

One should watch closely for the development of thrush. If this occurs, fluconazole (5 mg/kg PO SID) has broad-spectrum activity and is effective for many *Candida* spp.

The following table provides suggested dosages for **neonatal foals (<2 weeks) only – dosages often differ from those recommended for adults and older foals.**

Agent	Preparation	Route	Frequency (h)	Dosage (/kg)
Amikacin	sulfate	IV or IM	24	25 mg
Gentamicin	sulfate	IV, IM	24	12 mg
Ampicillin	sodium	IV, IM	6	25 mg
Penicillin G	potassium	IV	6	22,000-40,000 IU
	procaine	IM	12	22,000 IU
Cefotaxime	sodium	IV	6	40 mg
Ceftiofur	sodium	IV, IM	12	5 mg
Cefpodoxime	proxetil	PO	8	10 mg
Chloramphenicol	palmitate or base	PO	6 or 12 (if ≤5d)	50 mg
	sodium succinate	PO	6 or 12 (if ≤5d)	25-50 mg
Metronidazole		PO	25	12 mg

Cardiovascular support

Cardiovascular support is critical in foals with hypovolemia, acid-base disorders, septic shock or hypotension. When a foal presents in septic shock, fluid resuscitation is critical. Initial choices commonly include a combination of crystalloid and colloid preparations. In lieu of advanced monitoring, physical parameters, such as development of edema, urine output, vital signs, and temperature of the distal limbs, should be examined carefully during therapy.

Anti-acid therapy

Uncommonly, sick foals can develop gastric ulcers in the non-glandular or glandular region of the stomach. The use of prophylactic anti-acid therapy is controversial and highly dependent upon clinician preference. Severely ill, predominantly recumbent patients frequently have predominantly alkaline pH patterns and than their normal cohorts. Thus, glandular ulcer disease in sick neonates is likely not a strictly an acid-related problem and factors such as alterations in mucosal perfusion may contribute. In addition, gastric alkalinization may contribute to bacterial translocation. In situations where acid suppression is indicated (such as need for long-term NSAID use or documented ulceration), primary options for acid suppression in the neonatal foal include omeprazole and ranitidine. Sucralfate remains a possible alternative for ulcer prophylaxis, especially in foals receiving non-steroidal anti-inflammatory drugs, without altering intragastric pH.

Immunoglobulin therapy

Foals with documented failure of transfer of passive immunity should be treated with either plasma or colostrum, depending upon the timing. Foals with a serum IgG concentration less than 400 mg/ dL generally require intervention with colostrum or a commercial oral IgG product if less than 12-18 hours of age, or with intravenous plasma thereafter. Foals with a serum IgG between 400 and 800 mg/ dL should receive intervention if other factors are present that may predispose to disease, such as prematurity, dysmaturity, overcrowding, other diseased foals on the farm, or early signs of sepsis.

Colostrum quality should be ensured prior to administration. Good quality colostrum should have an IgG concentration greater than 3000 mg/dl, which is typically reflected by a colostrum specific gravity greater than 1.060 (colostrometer), a reading of >23% on a sugar refractometer or >16% on an alcohol refractometer. Commercially available frozen equine plasma offers a convenient source of plasma free of alloantibodies and infectious agents. Generally, administration of 1 liter of plasma will result in a 200-300 mg/dL increase in serum IgG in a 50-kg foal.

FOCAL INFECTION AND POTENTIAL SEQUELAE

Common focal infections include pneumonia (either hematogenous or aspiration), diarrhea, omphalitis, orthopedic infections, and meningitis. In foals with suspected omphalitis, ultrasonographic evaluation of the internal structures is critical, as external signs are frequently absent. Patent urachus can develop without involvement of other structures and will often resolve with antimicrobial therapy. Orthopedic infections represent one of the most important life-threatening and performance-limiting complications associated with sepsis. Clinical signs include lameness and joint effusion, and any such abnormality in a neonate should be considered septic until proven otherwise.

Meningitis is a rare but extremely serious complication. Major clinical signs include seizures and severe depression, although the latter is somewhat difficult to assess in a severely compromised foal. Other signs include head tilt, strabismus, nystagmus, and extensor rigidity, depending upon the areas of involvement. CSF culture and cytology will confirm the diagnosis, as affected foals will typically have a neutrophilic pleocytosis. Prognosis is poor to grave. The major differential diagnosis for neurological signs in a septic neonate is neonatal encephalopathy (NE). Typically foals with NE present within 24-48 hours following birth, whereas the age of foals with meningitis is more variable.

The most common ocular complications in the septic foal are corneal ulceration and uveitis. Disorders of coagulation are manifested clinically by either hemorrhage or thrombosis. The most common abnormality is jugular venous thrombosis, but brachial, digital, metatarsal, and metacarpal arterial and diffuse vascular thromboses have been reported.

PROGNOSIS/OUTCOMES

Most retrospective reports cite short-term survival for hospitalized septic neonates in the range of 70%.^{1,4,8,9} Various factors have been associated with short-term survival, but have not necessarily been consistent between studies.

Few studies have addressed the long-term survival and performance of neonatal intensive care unit survivors, much less septic foals specifically. At UF, no significant difference was demonstrated between 102 surviving Thoroughbred foals and 194 of their maternal siblings in percent starters, percent winners, or number of starts, but affected foals had significantly lower number of wins, total earnings, and standard starts index (SSI) than siblings.⁹

REFERENCES

1. Brewer BD, Koterba AM (1990), Bacterial Isolates and Susceptibility Patterns in Foals in A Neonatal Intensive-Care Unit, *Compendium on Continuing Education for the Practicing Veterinarian* 12: 1773-1781

2. Brewer BD, Koterba AM, Carter RL, Rowe ED (1988), Comparison of empirically developed sepsis score with a computer generated and weighted scoring system for the identification of sepsis in the equine neonate, *Equine Vet.J.* 20: 23-24
3. Corley KTT, Furr MO (2003), Evaluation of a score designed to predict sepsis in foals, *Journal of Veterinary Emergency and Critical Care* 13: 149-155
4. Gayle JM, Cohen ND, Chaffin MK (1998), Factors associated with survival in septicemic foals: 65 cases (1988- 1995), *J.Vet.Intern.Med.* 12: 140-146
5. Henson S, Barton MH. Bacterial isolates and antibiotic sensitivity patterns from septicemic neonatal foals: A 15 year retrospective study (1986-2000). Proc Dorothy Havemeyer Foundation Neonatal Workshop 3 [3], 50-52. 2001.
6. Marsh PS, Palmer JE (2001), Bacterial isolates from blood and their susceptibility patterns in critically ill foals: 543 cases (1991-1998), *J.Am.Vet.Med Assoc.* 218: 1608-1610
7. Paradis MR (1994), Update on Neonatal Septicemia, *Vet Clin.North Am Equine Pract* 10: 109-135
8. Russell C, Axon J, Blishen A, Begg A (2008), Blood culture isolates and antimicrobial sensitivities from 427 critically ill neonatal foals, *Aust.Vet J* 86: 266-271
9. Sanchez LC, Giguere S, Lester GD (2008), Factors associated with survival of neonatal foals with bacteremia and racing performance of surviving Thoroughbreds: 423 cases (1982-2007), *J.Am.Vet Med.Assoc.* 233: 1446-1452
10. Wilson WD, Madigan JE (1989), Comparison of bacteriologic culture of blood and necropsy specimens for determining the cause of foal septicemia: 47 cases (1978-1987), *J.Am.Vet.Med.Assoc.* 195: 1759-1763