The most common effects of perinatal asphyxia are:

- **Neurologic deficits** ranging from hypotonia to grand mal seizures
- **Gastrointestinal (GI) disturbances** ranging from mild ileus and delayed gastric emptying to severe, bloody diarrhea and necrotizing enterocolitis
- **Renal compromise** accompanied by varying degrees of oliguria

*Updated by the author and reprinted with permission from Standards of Care: Equine Diagnosis and Treatment 2002;2.1:1-7.
*Dr. Vaala discloses that she is employed by Intervet/Schering-Plough Animal Health.
Based on the neurologic deficits (including loss of affinity for the dam, seizures, impaired sucking and swallowing reflexes, and abnormal vocalization), affected foals have been called dummies, convulsives, barkers, and wanderers. Neonatal encephalopathy, neonatal maladjustment syndrome, and hypoxic-ischemic encephalopathy are commonly used to describe this condition. Central nervous system (CNS) disturbances associated with this condition ultimately result from necrosis and occasional hemorrhage.

During severe in utero compromise, there is sequential loss of fetal reflexes, with the most oxygen-demanding fetal activities disappearing first. Fetal reflexes are lost in the following order:

1. Fetal heart rate reactivity (the ability to increase heart rate in response to fetal activity)
2. Fetal breathing
3. Generalized fetal movements
4. Fetal tone

These biophysical events, in addition to amniotic fluid volume estimation and placental integrity, can be evaluated in late pregnancy using transabdominal ultrasonography.

**Diagnostic Criteria**

**Historical Information**

- No sex or breed predilection.
- Signs of peripartum asphyxia during the first 24 to 72 hours of life.
- Delivery may be outwardly normal in cases in which prepartum asphyxia is due to some form of unrecognized placental insufficiency and in utero hypoxia. Events during delivery that are associated with hypoxia include the following:
  - Dystocia
  - Premature placental separation (“red-bag” delivery)
  - Twinning
  - Meconium staining of fetal fluids, placenta, and/or foal
  - Evidence of diffuse placental pathology, including an unusually heavy or edematous placenta (e.g., placental weight >10% to 11% of the foal’s birth weight).
  - Mares with reproductive tract disease (e.g., placentitis, hydrops allantoi, hydrops amni, prepubic tendon rupture) are more likely to deliver affected foals. Severe maternal illness accompanied by anemia, hypoproteinemia, or endotoxemia can alter uteroplacental blood flow, resulting in fetal asphyxia. Postterm pregnancies have been associated with varying degrees of placental insufficiency and the birth of small, underweight, maladapted foals.
- Foals may appear normal at birth and then develop a host of behavioral abnormalities, including the loss of coordinated swallowing and sucking reflexes, the inability to locate the udder, the tendency to wander from the mare and walk into walls, generalized hypotonia, and seizures.

**Physical Examination Findings**

- **Mildly affected foals** exhibit jitteriness and hyperexcitability.
- **Moderately affected foals** exhibit stupor, somnolence, lethargy, and hypotonia, which may be accompanied by epileptiform seizures and extensor rigidity. Additional clinical signs include dysphagia, decreased tongue tone, odontoprisis, central blindness, mydriasis, anisocoria, nystagmus, head tilting, and loss of the suckle reflex.
- **Premature foals** are more likely to experience “subtle seizures” characterized by paroxysmal events, including eye blinking, eye deviation, nystagmus, pedaling movements, a variety of oral–buccal–lingual movements (e.g., intermittent tongue protrusion, sucking behavior), whole body thrashing, and other vasomotor changes (e.g., apnea, abnormal breathing patterns, changes in heart rate). Tonic posturing is another subtle seizure activity characterized

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**Thiamine**

Thiamine (1–20 mg/kg q12h) can be added to IV fluids to help preserve aerobic brain metabolism. Thiamine deficiency has been associated with intracellular and extracellular edema and neuronal cell death due to glutamate-induced, NMDA receptor-mediated excitotoxicity and compromised mitochondrial function.

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**Critical Point**

Foals may appear normal at birth and then develop a host of behavioral abnormalities, including the loss of coordinated swallowing and sucking reflexes, the inability to locate the udder, the tendency to wander from the mare and walk into walls, generalized hypotonia, and seizures.
by symmetric limb hyperextension or flexion
and is often accompanied by abnormal eye
movements and apnea.

- **Severely affected foals** exhibit marked
  CNS depression, coma, and loss of central
  regulation of respiration, blood pressure,
  and temperature, ultimately leading to death.
- Limb deficits and generalized spasticity are
  less common.
- Signs of renal compromise include
  decreased urine production with subse-
  quent peripheral edema formation.
- The GI tract is often affected. Mild cases
  may involve transient ileus, constipation,
  and mild colic. The most severe form of
  intestinal dysfunction is necrotizing entero-
  colitis. During GI ischemia, mucosal cell
  metabolism diminishes and production of
  the protective mucous layer ceases, allow-
  ing proteolytic enzymes to begin autodiges-
  tion of the mucosal barrier. Bacteria within
  the lumen can then colonize, multiply, and
  invade the bowel wall. Intramural gas is
  produced by certain species of bacteria, and
  *pneumatosis intestinalis* develops. Possible
  complications include intestinal rupture,
  pneumoperitoneum, severe bacterial perito-
  nitis, and septicemia.

### Laboratory Findings

**TABLE 1** lists clinical signs associated with
specific organ system dysfunction and the
laboratory abnormalities to anticipate.

- **Metabolic acidosis**: pH <7.3; bicarbonate
  concentration <20 mEq/L.
- **Prepartum placental insufficiency** may be
  associated with neonatal azotemia: creati-
  nine concentration >3.5 mg/dL.
- **Foals experiencing respiratory depression**
  may develop hypoxemia and respiratory aci-
  dosis: Po₂ <60 mm Hg; Pco₂ >65 mm Hg.

### Other Significant Diagnostic Findings

Transabdominal ultrasonography of the preg-
nant mare should be used to evaluate fetal
well-being and placental integrity:

- The mare’s ventral midline must be cleaned
  and clipped from the level of the umbilicus
  caudally to the mammary gland, and a vis-
  cious coupling gel should be applied.
- Minimal maternal restraint is usually
  required. Chemical sedation should be
  avoided because drugs such as xylazine
  and detomidine induce fetal bradycardia
  and decrease fetal movement.
- **A 2.5- to 3.5-MHz transducer** is used.

 Signs suggestive of fetal or placental com-
promise during the last month of gestation
include the following:

- **Persistent fetal bradycardia**: fetal heart
  rate <50 to 60 bpm; loss of fetal heart rate
  variability
- **Reduced or absent fetal movement** for pro-
  longed periods (>30 min)
- **Decreased volume of fetal fluids**: maximum
  ventral fetal fluid pocket depths average 8
  cm for amniotic fluid and 13 cm for allan-
  toic fluid
- **Large areas of placental separation**
- **Generalized placental thickening**: combined
  uteroplacental thickness >15 mm

 Transrectal measurements of uteroplacen-
tal thickness around the cervical star should
not exceed 12 mm after day 330 of gestation.

 Foals with necrotizing enterocolitis have
  generalized ileus and thickening of the bowel
  wall with or without intramural gas accumu-
  lation visible on transabdominal ultrasono-
  graphy when a 5- to 7.5-MHz transducer is used.

### Summary of Diagnostic Criteria

- **History of abnormal periparturient events**, including fetal compromise on
  ultrasonography, gross placental abnormali-
  ties, or delivery complicated by dystocia;
  premature placental separation; or meco-
  nium staining.
- **Development of neurologic deficits** in
  the newborn foal within the first 24 to 72
  hours of life; the most common CNS dis-
  turbances include hypotonia, loss of suckle
  reflex, loss of affinity for the dam, and focal
  or grand mal seizures.
- **No other obvious cause of CNS disease**, including septic meningitis, electrolyte dis-
  turbances, and trauma.
- **Hemogram and serum chemistries are**
  **often normal**, except for azotemia associ-
  ated with placental compromise and meta-
  bolic acidosis.
- **Foals experiencing severe dystocia** often
have elevated serum concentrations of the muscle-specific enzyme creatine kinase.

- The neonatal pancreas and liver can also sustain injury.
  - Foals with pancreatic damage may demonstrate insulin-responsive hyperglycemia.
  - Neonates sustaining hepatic injury may have elevated concentrations of the hepatocellular enzyme sorbitol dehydrogenase.
- Computed tomography and magnetic resonance imaging are newer modalities being used to evaluate CNS lesions.

Differential Diagnosis
Seizures during the first few days of life can be congenital or acquired. Causes of acquired seizures include the following:

- **Metabolic disorders:** Hypocalcemia, hypomagnesemia, hyponatremia, hypernatremia, hypoglycemia
- **Hyperosmolality:** Hyperlipemia, hyperglycemia
- **Severe azotemia
- Hepatoencephalopathy:** Elevated liver enzyme (aspartate aminotransferase, γ-glutamyltransferase, sorbitol dehydrogenase), serum ammonia, and bilirubin levels concurrent with low blood glucose and blood urea nitrogen levels

**Infectious conditions:**
- Bacterial meningitis
  - Spinal fluid analysis: leukocytes >5 to 10 cells/µL; total protein >150 mg/dL
  - Positive blood culture result
  - Abnormal hemogram results: leukopenia, neutropenia, toxic granules in neutrophils
- Viral meningitis associated with equine herpesvirus 1 infection
  - Positive presuckle viral titers
  - Virus isolation from buffy coat
  - Polymerase chain reaction testing using nasal swabs and buffy coat samples
- Cranial trauma

**Checkpoint**
Some experts disagree on the use of mannitol and DMSO for treating cerebral edema.

### TABLE 1  Clinicopathologic Conditions Associated with Perinatal Asphyxia Syndrome

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Clinical Signs</th>
<th>Laboratory Findings</th>
<th>Pathology/Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>Hypotonia, hypertonia, seizures, coma, loss of suckle reflex, proprioceptive deficits, apnea</td>
<td>Increased intracranial pressure, blood–brain barrier permeability, and albumin quotient</td>
<td>CNS hemorrhage, intracellular edema, ischemic necrosis</td>
</tr>
<tr>
<td>Renal</td>
<td>Oliguria, anuria, generalized edema</td>
<td>Azotemia, hyponatremia, hypochloremia, abnormal urinalysis results</td>
<td>Tubular necrosis, glomerular damage</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Colic, ileus, abdominal distention, bloody diarrhea, gastric reflux</td>
<td>Occult blood in the feces and reflux, <em>pneumatis intestinalis</em></td>
<td>Ischemic mucosal necrosis, enterocolitis, ulceration</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Respiratory distress, tachypnea, dyspnea, rib retractions</td>
<td>Hypoxemia, hypercapnia, respiratory acidosis</td>
<td>Hyaline membrane disease, atelectasis, meconium aspiration, rib fractures, pulmonary hypertension</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Arrhythmia, weak pulses, tachycardia, edema, hypotension</td>
<td>Hypoxemia, elevated myocardial enzymes</td>
<td>Myocardial infarct, valvular insufficiency, persistent fetal circulation</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Icterus, abnormal mentation</td>
<td>Hyperbilirubinemia, elevated liver enzymes</td>
<td>Hepatocellular necrosis, biliary stasis</td>
</tr>
<tr>
<td>Endocrine (adrenal and parathyroid glands)</td>
<td>Weakness, apnea, seizures</td>
<td>Hypocortisolemia, hypocalcemia</td>
<td>Necrosis, hemorrhage</td>
</tr>
</tbody>
</table>
Congenital causes of seizures include CNS malformations, including hydrocephalus, corpus callosum agenesis, cerebellar abiotrophy (most common in Arabians), hydranencephaly, and lavender foal syndrome (observed in Arabian foals of Egyptian lineage that have diluted coat color).

- Normal serum chemistry results help rule out metabolic disturbances.
- A normal leukogram or the absence of severe leukopenia, neutropenia, and toxic neutrophil changes may help rule out septic conditions.
- Cerebrospinal fluid (CSF) analysis is indicated if septic meningitis is a possible differential. Septic meningitis produces an increased nucleated cell count, protein concentration, and IgG index in the CSF. Brain damage may result in an increased albumin quotient in the CSF compatible with increased blood–brain barrier permeability.

### Treatment Recommendations (TABLE 2)

#### Initial Treatment

**Seizure Control**

- **Diazepam (0.11 to 0.44 mg/kg IV)**
  - Can repeat dose in 30 minutes
  - Rapid onset of action, but short duration of effect
  - Inactivated by plastic and sunlight
  - Avoid repetitive doses to reduce risk of respiratory depression

- **Phenobarbital (2 to 10 mg/kg slowly IV q8–12h)**
  - High doses and rapid rate of administration are associated with respiratory depression.
  - Infuse slowly over 15 to 20 minutes. Expect peak effect within 45 minutes.

#### Possible Treatments for CNS Cellular Damage

- **Mannitol (0.25 to 1.0 g/kg IV given as a 20% solution over 20 to 30 min q4–12h)**
  - May exacerbate severe intracranial hemorrhage.
  - Excessive administration may induce significant alterations in plasma osmolality. Monitor hydration status.

- **Dimethyl sulfoxide (DMSO; 0.5 to 1.0 g/kg IV given as a 20% solution slowly over 1 hr q12–24h)**
  - Use cautiously in hypotensive neonates.

- **Alternative route of administration is via nasogastric intubation but is not usually recommended in critically ill neonatal foals.**

#### Therapy for Central Respiratory Center Depression and Periodic Apnea

- **Caffeine (10 mg/kg PO or per rectum as initial loading dose, followed by maintenance dose of 2.5 to 3.0 mg/kg PO q24h)**
  - Helps increase carbon dioxide sensitivity of central respiratory center, leading to an increased respiratory rate
  - Most effective when hypercapnia has produced significant acidosis

- **In certain cases of persistent hypercapnia, positive pressure ventilation may be necessary.**

#### Broad-Spectrum, Bactericidal Antimicrobials to Treat and Prevent Secondary Sepsis

- **Amikacin (20 to 28 mg/kg IV q24h) and potassium penicillin (22,000 to 40,000 IU/kg IV q6h) or ampicillin sodium (20 to 50 mg/kg IV q6h); if amikacin is used, peak and trough monitoring is recommended.**

- **Ceftiofur (5 to 10 mg/kg IV q6–12h)**

#### Alternative/Optional Treatments

**Seizure control:**

- **Pentobarbital (2 to 10 mg/kg IV q4–8h or to effect)** is an alternative to phenobarbital. Long-term use is not recommended.

- **Midazolam (2 to 5 mg IM for a 110-lb [50-kg] foal)** can be given IV, but hypotension and apnea may occur following rapid IV administration. Use lowest effective dose.

- **Naloxone (0.01 to 0.02 mg/kg IV), an opiate antagonist, has been used to diminish CNS depression.**

- **Low doses of magnesium sulfate (50 mg/kg/hr diluted to 1% solution and given slowly IV as a constant-rate infusion for 1 hr, then decreased to 25 mg/kg/hr as a constant-rate infusion for up to 24 hr) may be considered.** Magnesium acts as an NMDA-receptor antagonist and may reduce the hypoxia-induced increase in oxygen free radical generation.

- **Ascorbic acid (vitamin C)** has been advocated as an antioxidant. It is believed to act as a neuromodulator that inhibits neurotransmitter binding to NMDA receptors. The optimal dose for neuroprotection has not been determined. Oral doses vary from 50 to 100 mg/kg/day.

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**Critical Point**

CSF analysis is indicated if septic meningitis is a possible differential. Septic meningitis produces an increased nucleated cell count, protein concentration, and IgG index in the CSF. Brain damage may result in an increased albumin quotient in the CSF compatible with increased blood–brain barrier permeability.


α-Tocopherol (vitamin E) has also been advocated for its antioxidant effect. Peroxyl radicals liberated during hypoxia-induced lipid peroxidation react with α-tocopherol instead of a free fatty acid, thereby terminating a potentially destructive process. The optimal dose of vitamin E has not been established. I have used 500 to 1000 U/day PO.

**Supportive Treatment**

- **Protect the foal from self-trauma during seizures.**
  - Provide a padded environment and soft, absorbent bedding.
  - Wrap limbs.
  - Apply artificial tears to the eyes to prevent secondary corneal ulceration.

- **Ensure adequate passive transfer of colostral antibodies.**
  - The foal’s serum IgG should be >800 mg/dL by 18 to 24 hours of age. If IgG is <800 mg/dL:
    - Give a minimum of 10 mL/kg of hyperimmune plasma IV if the foal is >18 to 24 hours of age or gut function is compromised.
    - Give a minimum of 40 g/kg IgG PO by bottle or nasogastric tube using good-quality colostrum or an artificial IgG supplement if the foal is <12 to 18 hours of age and has a functional gut.

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**Table 2: Drugs Commonly Used to Treat Foals**

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Clinical Signs</th>
<th>Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>Seizures</td>
<td>▶ Diazepam: 0.11–0.44 mg/kg IV&lt;br▶ Phenobarbital: 2–10 mg/kg IV q12h (give slowly, monitor serum level) or 2–10 mg/kg IV to effect&lt;br▶ DMSO: 0.5–1.0 g/kg IV as 20% solution over 1 hr; can be repeated q12h&lt;br▶ Mannitol: 0.25–1.0 g/kg IV as 20% solution over 15–20 min q12–24h</td>
</tr>
<tr>
<td>Renal</td>
<td>Oliguria, anuria</td>
<td>▶ Dobutamine infusion: 2–15 µg/kg/min; consider use if cardiac dysfunction is contributing to hypotension and poor renal perfusion</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Ileus, GI distention</td>
<td>▶ Erythromycin: 1–2 mg/kg PO q6h or 1–2 mg/kg/hr IV infusion q6h&lt;br▶ Cisapride: 10 mg PO q6–8h&lt;br▶ Metoclopramide: 0.25–0.5 mg/kg/hr CRI q6–8h or 0.6 mg/kg PO q4–6h&lt;br▶ Bethanechol: 0.03 mg/kg SC q8h or 0.16–0.2 mg/kg PO q8h</td>
</tr>
<tr>
<td></td>
<td>Ulcers</td>
<td>▶ Sucralfate: 20–40 mg/kg PO q6h&lt;br▶ Ranitidine: 5–10 mg/kg PO q6–8h or 1–2 mg/kg IV q8h&lt;br▶ Cimetidine: 15 mg/kg PO q6h or 6.6 mg/kg IV q6h&lt;br▶ Omeprazole: 4.0 mg/kg PO q24h (not labelled for use in foals &lt; 4 weeks of age)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Hypotension</td>
<td>▶ Vasopressin infusion: 0.25–1.0 mU/kg/min&lt;br▶ Dobutamine infusion: 2–15 µg/kg/min&lt;br▶ Digoxin: 0.02–0.035 mg/kg PO q24h if cardiac failure is suspected</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Hypoxemia</td>
<td>▶ Intranasal humidified oxygen insufflation: 2–10 L/min</td>
</tr>
<tr>
<td></td>
<td>Apnea</td>
<td>▶ Caffeine: Loading dose: 10 mg/kg PO&lt;brMaintenance dose: 2.5–3.0 mg/kg PO q24h&lt;br(Some experts prefer doxapram HCl instead of caffeine in neonatal foals.(^a)^)</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Hypocortisolemia</td>
<td>▶ Adrenocorticotropic hormone (depot): 0.26 mg IM q8–12h</td>
</tr>
<tr>
<td>Immune</td>
<td>Failure of passive transfer, leukopenia</td>
<td>▶ Hyperimmune plasma: 10–20 mL/kg IV; monitor serum IgG level and leukocyte count</td>
</tr>
</tbody>
</table>


Perinatal Asphyxia Syndrome in Foals

Provide adequate nutrition and monitor glucose level until the foal can nurse normally from the mare.

- Minimal nutritional requirement = 10% of the foal's body weight per day as milk fed as small meals every 1 to 2 hours (e.g., a 110-lb [50-kg] foal would require a minimum of 5 L or 11 pints of milk per day divided into 10 to 12 feedings per day).
- Offer milk by bottle if the foal has a strong suckle reflex and a coordinated swallow reflex.
- Tube feed by nasogastric intubation if the suckle or swallow reflexes are ineffective.
- Consider IV fluids supplemented with dextrose if the foal is inappetent; however, use parenteral nutrition if the foal is critically ill or has severe necrotizing enterocolitis.
- Continue to milk the mare every 2 to 3 hours until the foal can nurse normally.

Maintain cerebral perfusion, tissue perfusion, and blood pressure by administration of IV crystalloid fluids.

Patient Monitoring

- Perform serial neurologic evaluations to assess the response to treatment.
- Monitor vital signs (including blood pressure), manure and urine production, and peripheral pulses. If respiratory depression is present, check the arterial blood gases to assess pulmonary function and the need for oxygen therapy.
- Frequently monitor the blood glucose level.

Milestones/Recovery Time Frames

- Expect to see stabilization of CNS signs within the first 48 to 72 hours following delivery.
- Expect to observe gradual improvement in neurologic signs within the first 3 to 5 days.
- Some foals may not regain the ability to nurse from the mare for 7 to 10 days.

Treatment Contraindications

- Avoid acepromazine because it lowers the seizure threshold.
- Avoid xylazine because it causes transient hypertension that can exacerbate CNS hemorrhage.

Caution

Use caution and monitor renal parameters (creatinine and blood urea nitrogen levels, urinalysis) when administering potentially nephrotoxic medications (amikacin, flunixin meglumine) to critically ill neonatal foals.

Prognosis

With proper support, 70% to 80% of foals with this condition recover. Most foals recover completely, and many “survivors” perform successfully as racehorses and other athletes.

Foals with the poorest prognosis develop sepsis, fail to show any signs of neurologic improvement within the first 5 days of life, remain comatose and difficult to arouse, and experience severe, recurrent seizures. Dysmature and premature foals with prolonged in utero insult are more likely to have refractory hypotension and persistent subtle seizure activity than are full-term foals. Rare, long-term CNS sequelae include unusual docility as an adult, vision impairment, residual gait spasticity, and recurrent seizures.

Favorable Criteria

- A full-term foal experiencing a brief in utero or peripartum insult
- Minimal or mild GI and renal involvement
- A foal that is normal at birth, with CNS deficits developing within 12 to 24 hours of delivery

Unfavorable Criteria

- Advanced prematurity in addition to an in utero or peripartum insult
- Concurrent septicemia
- Severe necrotizing enterocolitis
- Nonresponsive hypotension and oliguria
- Persistent seizures that continue past 5 days of age despite anticonvulsive therapy
- A foal that is abnormal immediately following delivery and remains comatose and nonresponsive
- Signs of severe brainstem damage: loss of thermoregulatory control, profound apnea, marked increase in intraocular pressure suggestive of increased intracranial pressure.