Treatment strategies in the perinatal mare and foal

P.R. Morresey

Rood and Riddle Equine Hospital, PO Box 12070, Lexington, KY, USA

Abstract

A large number of conditions are recognized in the peripartum period that have the potential to impact the health and future performance of both the mare and the foal. Peripartum hemorrhage can be insidious in onset and result in profound abdominal pain, hypovolemia and in severe cases death of the mare. Those mares that survive the initial hemorrhage may succumb some time after the apparent stabilization of the hematoma. Treatment is aimed at promoting hemostasis and improving cardiovascular performance while not promoting further hemorrhage. Many drugs in common use have been chosen due to anecdotal reports of success or extrapolation from studies on horses or other species. Large, multi-center controlled trials of therapeutic agents are lacking, this being expected given the critical nature of the condition. The compromised neonatal foal is a challenge to the attending clinician, who must balance the immediate medical needs of the foal with the financial requirements of the client. Following the initial assessment, resuscitation of the neonate must be performed in a timely and efficacious fashion. The attending clinician should establish a coherent and consistent approach to cardiovascular resuscitation of the foal. Following this event, stabilization of the neonate and preparation for transport to a referral center if required can occur. A thorough knowledge of the expected neonatal development of the foal will aid in selection of foals requiring specialist intervention.

Keywords: Mare, peripartum, hemorrhage, foal, neonatal, resuscitation

Introduction

The peripartum period for both the mare and the foal can be a period of great risk to life and future potential. A myriad of problems exist, and it is beyond the scope of this presentation to cover them all. Therefore a selected few will be covered in detail: peripartum hemorrhage in the mare, neonatal foal resuscitation, stabilization and preparation for referral.

Mare

Considerations in the periparturient mare

The periparturient mare does not differ substantially from the non-pregnant mare with respect to general husbandry. Routine exercise, a balanced diet and regular preventative health care (teeth, deworming and vaccination) should all continue as before.

Differences become important when they involve the overall health of the mare and the effects on placental function that systemic illness can have. The goals of therapy should address resolution of the precipitating problem, systemic support for the mare (and therefore fetoplacental unit) and the avoidance of fetal hypoxia.

The overall health of the mare will be affected by any disease process resulting in inappetance, fever or proinflammatory mediator production with systemic release. Nutritional insult resulting in weight loss during mid-gestation has detrimental effects on placental development which results in reduced fetal growth.[1] Endocrine function of the foal is also affected.[2]

Colic is also of greater concern in the periparturient mare, as this condition presents a serious diagnostic challenge to the practitioner through limitations imposed upon examination by the presence of the gravid uterus. Accurate differentiation between gastrointestinal conditions and gestational accidents is essential but difficult in many cases. Early gastrointestinal problems can appear similar to initial stages of labor. Peripartum gastrointestinal conditions include large colon volvulus or displacement, cecal rupture, small intestinal volvulus, enterocolitis and direct trauma to the intestine.[3]

Trauma to the gut may result in ischemic necrosis of the affected areas.[4-6]. Compromise to the gastrointestinal tract results in the onset of endotoxemia with profound circulatory dysfunction and proinflammatory stimuli occurring. Serious metabolic insults can affect both the mare and concurrently the fetus. Treatment of the gastrointestinal disease may involve general anesthesia with abdominal exploration further insulting the fetoplacental unit.

Hypoglycemia of the mare resulting from inappetance or fasting while colic treatment continues decreases glucose delivery to the fetus. Administration of glucose to late-term pregnant mares is recommended to avoid this, as is supplementation of feed material by nasogastric intubation where practical. Oxygen therapy is also recommended where placental function is suspected to be compromised.[7]

Reproductive problems in the peripartum period with apparent colic as a presenting clinical sign include uterine torsion, uterine rupture, uterine laceration, uterine bruising and hemorrhage of the blood vessels supplying the reproductive tract.[3]

Peripartum hemorrhage

Rupture of and subsequent hemorrhage from the uterine artery is the most common cause of death in mares *post partum.*[3] The external iliac artery, utero-ovarian artery, and uterine artery have also been implicated.[8] In a review of central Kentucky mares, reproductive complications accounted for the majority (57 of 98 cases, 58%) of deaths in peripartum mares.[9] Of those that died of reproductive complications, rupture of a uterine artery was determined to be the cause of death in 40 cases (70%). The incidence of peripartum hemorrhage in the mare has not been determined by retrospective studies of large numbers of mares, instead reports of clinical cases are found in the literature. Hemoperitoneum itself is a significant cause of abdominal discomfort in the horse, with approximately 13% of all cases due to rupture of uterine vessels.[10]

Although usually considered a problem of the post partum period, a number of reports exist of cases in the prepartum period.[8,11] Peripartum hemorrhage has been reported to occur at any age, however older mares are considered to be at greater risk.[12] Age-related degeneration of arterial vessels associated with the reproductive tract is suspected to be the reason for the increased incidence in older mares, coupled with the increased mechanical stresses imposed by the gravid uterus. Uterine contractions and obstetrical manipulations further increase stress on the vessel wall.[13] Copper deficiency was identified as a contributing factor in mares experiencing fatal hemorrhage, whereas non-fatal hemorrhage mares had comparable copper levels to their non-affected cohorts.[14]

Peripartum hemorrhage can occur in any of the following forms: hemorrhage into the peritoneal cavity, hemorrhage retained either within the broad ligament of the uterus or within the uterine wall (mural hemorrhage) or hemorrhage into the uterine lumen. Combinations of these may occur, necessitating thorough evaluation of mares affected by

seemingly less serious forms of hemorrhage so as to avoid non detection of life-threatening episodes.

Hemorrhage into the peritoneal cavity can lead to profound hypovolemia, pain and result in peracute death. If confined to the broad ligament or uterine wall, pain can still be significant but prognosis for life is better. These hematomas may be incidental findings during routine reproductive examinations, or may become acutely apparent some time after foaling following the onset of abdominal hemorrhage. Hemorrhage within the uterine lumen is usually of less significance due to the relatively small amount of blood lost from the circulating pool in most cases.

Diagnosis

Clinical parameters of horses experiencing acute blood loss and hemoperitoneum have been reviewed.[10,15] Consistent signs included depression, tachypnea, tachycardia, poor pulse quality, pale mucous membranes, prolonged capillary refill time, cool extremities and abdominal discomfort. Signs occurring less often included abdominal distention, sweating, ataxia, and a mass in the broad ligament palpated *per rectum*.

Clinical pathology findings include anemia, neutrophilia, lymphopenia, thrombocytopenia, hypoproteinemia, hypocalcemia, and azotemia. Measurements of hemostasis (prothrombin time, parital thormoboplastin time, template bleeding time) are usually normal.

The diagnosis of hemoperitoneum is confirmed by transabdominal ultrasonography and abdominocentesis. Lesions at necropsy may include a ruptured miduterine artery or ruptured broad ligament hematoma. On occasion, the source of hemorrhage may be the iliac vessels.

Rectal examination is controversial, with the need to make a diagnosis balanced by the concern of worsening hemorrhage. There is no evidence that rectal examination of mares suffering prepartum hemorrhage adversely affects outcome.[12] Rectal examination may not aid diagnosis, as the hemorrhage may dissect between tissue planes and not form a discrete, palpable mass in the broad ligament. Careful transrectal ultrasonography may greatly aid diagnosis due to the ability to detect non-palpable lesions.

Treatment

Due to the sporadic nature of the condition, treatment modalities are derived by extrapolation from studies on humans, laboratory species and anesthesia studies in the horse. A number of treatments have been recommended, with both scientific and anecdotal backing for those in common usage:

ε-aminocaproic acid. The effects of ε (epsilon) aminocaproic acid (EACA) on coagulation and fibrinolysis in healthy horses have been reviewed.[16,17]. Partial thromoplasin time (PTT) was found to be significantly decreased and α_2-antiplasmin activity was significantly higher. Fibrinogen was significantly lower than baseline. Bolus dosage is more practical in field situations; however a recent review[17] established an efficacious constant rate infusion protocol.

The procoagulant EACA is a synthetic anti-fibrinolytic amino acid. Similar agents are widely used in human medicine to arrest hemorrhage. The lysine binding sites of plasminogen become saturated with EACA which displaces plasminogen from the fibrin surface stabilizing the hemostatic plug.[18]

Naloxone. Naloxone is anecdotally reported and widely used in the treatment of postpartum mare hemorrhage.[3] Experimental evidence shows that endorphins released

by stress act on opiate receptors to depress cardiovascular function during hemorrhagic shock.[19] Naloxone acts as a μ-opioid receptor competitive antagonist and also has (lesser) antagonist action at the κ- and δ-opioid receptors. The hemodynamic effects of blood loss were shown to be ameliorated by intravenous administration of naloxone as evidenced by an increase in arterial pressure, left ventricular function and cardiac output.[20,21] Regional blood flow differences were noted in the dog, with naloxone improving circulation to the myocardium, intestine, liver and adrenal.[22] In the horse, naloxone (0.20 mg/kg iv) immediately following acute hemorrhage was found to counter the increase seen in heart rate.[23] However, this would result in a considerably higher dose than that commonly in usage (8 mg) for the hemorrhaging mare. At available concentrations (0.4 mg/ml) a volume of 250ml would have to be infused to achieve the higher dose rate shown to be effective in acute hemorrhage situations.

Dexamethasone or other corticosteroids. The beneficial effects of dexamethasone administration during hemorrhagic shock has been shown in dogs.[24,25]. Increased mean arterial pressure was noted, as was improved blood flow to the pulmonary, gastrointestinal and renal circulations. Furthermore, less cell damage was evident as shown by decreased plasma enzyme elevations referable to damaged tissues.

Formalin. Formalin activation of platelet function during fixation *in vitro* has been reported.[26] The procoagulant properties of formalin (aqueous formaldehyde) in the horse have been critically reviewed.[27] In spite of a reported decrease in clotting and bleeding time in goats,[28] administration was shown to have no effect on primary or secondary hemostasis in normal or aspirin-treated horses.[27] Behavioral effects, tachycardia, lacrimation, salivation and muscle fasciculations were seen at higher doses.

Despite no effect on coagulation seen in that study, the usage of intravenous formalin for its purported hemostatic properties is widely practiced in equine medicine.

Yunnan baiyao. Yunnan Baiyao (or Yunnan Paiyao, literally white medicine from Yunnan) is a hemostatic powder of largely unknown constituents. Purported uses include hemostasis, relief of pain, diminishment of swellings and the improvement of circulation to the tissues. The mechanism of action is unknown. Experimentally, template bleeding time of halothane anesthetized ponies was decreased when compared to baseline values following the administration of yunnan baiyao 4 h prior to and immediately preceding induction of anesthesia.[29] Activated clotting time was not affected in this study. Anecdotal reports indicate widespread usage by equine practitioners with reported favorable results.

Acepromazine. The pharmacokinetics and pharmacodynamics of intravenous acepromazine have been extensively reviewed in the horse.[30,31] Use in the hemorrhaging mare is controversial as concerns are held for the potential exacerbation of hypovolemia. However, use allows the hypotensive restoration of adequate circulatory blood volume with a diminished chance of dislodging the hemostatic plug.

Butorphanol. Butorphanol tartrate is widely used for control of pain and chemical restraint in the hemorrhaging mare. Concurrent judicious use of the α_2 adrenergic agonists (xylazine, detomidine) further aids in control of anxiety. Butorphanol is a partial agonist/antagonist at the μ opioid receptor and an agonist at the κ opioid receptor. Therefore, potential for antagonism exists with the concurrent usage of butorphanol and naloxone.

Blood transfusion. Whole blood is the fluid of choice in cases of hemorrhagic shock. However, this is often not available; therefore isotonic polyionic solutions are administered to maintain circulating volume, with consideration of their relatively short time within the vascular space. When blood is lost from the intravascular compartment, central venous pressure decreases and blood lactate concentration increases significantly when compared with baseline values in the healthy horse.[32,33] Surprisingly, heart rate and venous blood gas analysis do not change significantly in the initial period. Therefore, blood lactate concentration is a useful measure of hypovolemia in horses in situations of acute loss before other parameters become abnormal. Also, it may be useful to indicate the need for blood transfusion and monitor responses of horses when whole blood is administered.[32]

Plasma. The administration of plasma is widely practiced for the provision of clotting factors and oncotic support to the hemorrhaging mare. This is useful in situations where anemia is severe once the mare is stabilized and whole blood is not available. In an emergency situation, this is less practical as plasma needs to be administered slowly and the benefit of administration will not be realized in a clinically relevant time frame. Volumes in common usage (1 L) are unlikely to measurably affect oncotic pressure and hemodynamic performance.

Hypertonic saline. In situations of acute blood loss, the restorative fluid used is of lesser importance as long as an appropriate volume is given.[34] In human medicine, considerable interest has been shown in the use of hypertonic saline dextran (HSD) in situations where significant hemorrhage has occurred.[35] Controversy still surrounds the use of hypertonic solutions for rapid restoration of intravascular volume.[36] In the

hemorrhaging mare, use of hypertonic saline is widely practice but similarly controversial due to the possibility of rapid plasma volume expansion causing a deleterious rapid spike in blood pressure.

Hetastarch. Hetastarch, 6% hydroxyethyl starch solution, is an artificial colloid used as a plasma volume expander. It has oncotic activity only and is not a blood or plasma substitute. Hetastarch is elimintated over a prolonged period by the kidneys. In situations where rapid plasma volume expansion is needed, hetastarch can be given as a series of rapid bolus doses in contrast to plasma which must be slowly administered. For this reason it offers an attractive way to rapidly ameliorate the effects of acute blood loss. However, one retrospective study suggests that intraoperative use of hetastarch in human cardiac surgery may increase bleeding and subsequent blood transfusion requirements.[37]

Polyionic replacement fluids. Volume restoration by polyionic fluids is widely practiced in the hemorrhaging mare. These fluids rapidly leave the vascular space (30 minutes) and do not provide a long term solution to hypovolemia, but instead provide a rapid transient means to combat blood loss. When used in conjunction with colloids (plasma and hetastarch) or hypertonic saline a more prolonged effect can be expected. Care must be taken to avoid overzealous plasma volume expansion to preserve the hemostatic plug.

Lidocaine infusion. The historical use of lidocaine as a systemically administered analgesic for intractable human pain has been reported.[38] Analgesic effects in horses have only been relatively recently reported.[39] When practical, a constant rate infusion of lidocaine is an excellent analgesic for the hemorrhaging mare, especially if hemoperitoneum is present. An appropriate dosage regimen is an initial lidocaine

loading dose (1.3 mg/kg iv) as a slow bolus, followed by a constant rate infusion (0.05 mg/kg/min iv), preferably using a fluid pump however this is not essential.

Management

Although controversy exists as to the utility of various therapeutic agents, ensuring the mare is as calm as possible and not exposed to undue stress is widely agreed upon. Care should be taken during restraint to not excessively stress the mare by using a combination of physical and chemical restraint.

Broad spectrum antimicrobial therapy is indicated to prevent the establishment of bacterial overgrowth in any hematomas or stagnant pools of blood post hemorrhage. Anti-inflammatory therapy should be maintained following the initial insult to minimize pain and distress, which may lead to increased blood pressure and restarting of hemorrhage.

Fluid therapy should be approached with caution and closely monitored. Rapid plasma volume expansion can lead to hemodilution, loss of the hemostatic plug and restarting of hemorrhage. This must be weighed against the necessity of restoration of an adequate circulating volume in the hypovolemic mare. The mare will succumb to hypovolemia not anemia in the acute phase of blood loss.[34] The signs of hemorrhage and hypovolemia are well known: visible distress or colic signs, muscle fasciculations, sweating along the flanks, flehmen, elevated heart and respiratory rates, and palor of the mucous membranes. Should these signs return during fluid restoration, an immediate decrease in the rate of admission should be considered. In the healthy horse, where potential for hemorrhage is not present, one-half of the calculated fluid deficit can be administered rapidly, with the remainder of the deficit given over the ensuing 24 h.

However, in the mare affected by peripartum hemorrhage, this initial rapid high volume administration is not possible.

A representative treatment plan for the author follows. Subsequent to the diagnosis of hemorrhage, an intravenous catheter is placed and an initial 5 L bolus of polyionic fluids containing 20 g ε-aminocaproic acid as a hemostatic agent is given over 30 min. Concurrent with this, acepromazine is administered intramuscularly to allow hypotensive circulating volume restoration and to act as a mild calming agent. Unless the mare is showing obvious signs of cardiac compromise, naloxone is not administered. Broad spectrum antimicrobial coverage is initiated (K penicillin and gentamicin, alternatively trimethoprim-sulfamethoxazole) for a minimum of five d. Analgesia and anti-inflammatory therapy is provided by flunixin meglumine. When this is insufficient, a constant rate infusion of lidocaine is given until 48 h following the last noted abdominal pain. Hemostatic therapy is continued for 2 to 3 d, allowing ultrasonographic evidence of the cessation of hemorrhage and stabilization of the hemorrhage site (if visible or palpable) to be noted. The author avoids the use of oxytocin in post partum hemorrhage mares, and is judicious with rectal evaluation. Uterine lavage, when attempted after 2 to 3 d, involves the establishment of a siphon and avoids distension of the uterus whenever possible. Undue stress from any source is avoided. This is especially important with mares protective of the foal, where procedures involving the foal are minimized and absences will be avoided if at all possible.

An appropriate fluid plan following stabilization of the hypovolemic mare is to provide a maintenance rate of polyionic intravenous fluids (2 ml/kg/h) until water intake is deemed sufficient. A PCV that is low but stable is acceptable. The author considers a

PCV of 15% that is stable acceptable, however a blood cross match is initiated at this point. The PCV will begin to slowly rise (1 to 2% daily) once hemorrhage ceases and the bone marrow responds. Resorption of peritoneal blood (if present) aids in this increase.

Should the mare reach a PCV of 12% and continue to decrease, up to 20% of the mare's circulating volume should be replaced with whole blood over 2 to 3 h by transfusion from a compatible donor. In this case, it should be expected that the PCV will begin to slowly decrease again over a period of 2 to 3 d as the transfused red blood cells are removed from circulation.

Useful drug dosages for postpartum mares are summarized in Table 1.

The Foal

Peripartum risk factors

Peripartum factors affecting the neonatal foal may be divided into three broad categories.

Maternal health. Systemic illness with fever, gastrointestinal compromise (potential for endotoxemia), and surgical manipulation are deleterious to the fetus. Nutritional status also affects fetal health.[1]

Reproductive conditions of the mare. History of previous neonatal compromise, known placental pathology (infection, thickening, separation), abnormalities of the birth canal, vulvar discharge, and loss of colostrum prepartum alert the clinician to potential neonatal difficulties.

Parturient events. The neonate can be affected by an abnormal gestation length, prolonged labor, dystocia, premature placental separation, and premature rupture of the umbilical cord. Meconium aspiration leads to hypoxic injury and pulmonary disease,

with presence of meconium in the amniotic fluid or amnion sometimes the only indication of this event.

Resuscitation of the compromised neonate

Prior preparation in anticipation of an emergency is paramount to success. A readily available collection of necessary equipment and drugs, kept within an easily accessible and portable container aids in achieving a successful outcome. A list of drug dose rates useful in resuscitation situations should be kept within the drug kit (Table 2).

Preparation of the foal for resuscitation includes drying and generally stimulating the neonate, and clearance of respiratory and oral secretions by suctioning to maximize the airway. It is convenient and safest to position the foal in lateral recumbency with any rib fractures down.

ABCDE of resuscitation

Establishing a clear and consistent protocol for resuscitation of the neonate is important when seeking to avoid delays in action during emergency situations (Table 3). The order of activities can easily be remembered by the ABCDE protocol. Techniques, drug dosages and break points determining changes in action may vary between individual clinicians due to preference and case experience. The aim of establishing a regular and sustainable cardiac and respiratory rhythm however is common to all protocols.

Indications for referral

The normal newborn foal displays a fairly predictable progression from the time of delivery to the onset of appropriate foal behavior and physiology (Table 4).

Significant deviation from these benchmarks strongly suggests that referral for advanced care should be considered.

Evaluation of the *at risk* foal includes a physical examination and consideration of the gestational history and laboratory values if available (Table 5). Although the foal may appear normal initially, rapid deterioration is possible and subtle deviations in physical findings and blood values may be the only indication of impending trouble.

Stabilization of the foal and preparation for referral

If the foal is showing signs of distress it may be prudent to transport the foal as soon as possible even if separately from the mare. Send colostrum from the mare for later administration and the placenta for examination if available.

If hypothermic, ensure the foal remains warm. Use blankets, insulated foal covers, or provide external sources of heat such as warmed fluid bags. Avoid excessively warming the hypovolemic foal as increasing circulation at the periphery can lead to profound falls in blood pressure.

If breathing difficulties are present, place an intranasal oxygen cannula. Insert the tip to the level of the eye socket. Portable oxygen tanks can be set to provide 5L oxygen flow per minute.

Fluids should be administered if dehydration or hypovolemia are present. Half the calculated deficit (deficit in liters = bodyweight in kg x % dehydration) can be given rapidly prior to referral. Maintenance fluid rates for foals are higher than the adult horse, being 5% to 10% of body weight daily, i.e., 2 to 4 ml/kg/hr. When calculating the required maintenance rate, consider all sources of fluid intake for the foal to avoid over hydrating the compromised foal. This is especially important if the foal is recumbent as

exceeding 10% of bodyweight can promote pulmonary edema formation. Glucose supplementation (2.5% or 5% dextrose in polyionic fluids) can be given if blood glucose levels are low, however rapid rehydration of the foal should always use non-glucose containing fluids. Care must be exercised with the addition of glucose to fluids as over supplementation results in hyperinsulinemia and subsequent worsening of hypoglycemia.

Placement of an indwelling feeding tube will aid in administration of colostrum as well as provide a vehicle for continued feeding of the foal (if appropriate) during transport to the referral facility should this be distant from the farm. Ensure the foal is fed standing (if able to rise) or only when in sternal recumbency. Reflux of gastric content is still possible with a correctly placed nasogastric tube. Avoid overfeeding the sick foal: a useful rule of thumb is to feed 10% of the bodyweight of the foal as milk over a 24 h period. Divide this amount into 12 equal feeds at two h intervals. Should colic or nasogastric reflux occur post feeding, discontinue immediately.

Antimicrobial therapy should not be delayed in the foal suspected of sepsis (Table 2). Collection of a blood culture using aseptic technique before administration of antimicrobials is desirable to improve chances of yielding the causative infectious agent. This can be shipped with the foal for bacteriologic examination and antimicrobial sensitivity analysis.

Anti-inflammatory treatments are also indicated in the foal that has sustained physical trauma or is febrile. Lipid derived inflammatory mediators are important in the pathophysiology of hypoxic ischemic encephalopathy (HIE) suggesting prompt use of non-steroidal anti-inflammatory drugs (NSAIDs) and anti-oxidant therapies is warranted. The NSAIDs vary in their potential for gastric mucosal and renal toxicity, especially if

used in the dehydrated patient; therefore care must be exercised in selection for the compromised neonate.

If neurological dysfunction is present, control of cerebral edema and seizure activity (if present) are indicated. Cerebral edema results from any traumatic, ischemic or hypoxic insult to the neonate. The onset of signs of neurological dysfunction is usually delayed, becoming apparent after a 24 to 48 h period of apparently normal development. Often the only suggestions of impending problems are the gestational history, parturient events, and subtle early neonatal behavioral abnormalities. Should seizure activity ensue, control of seizure activity in the first instance is necessary to avoid rapid exhaustion of the foal and secondary injuries predisposing to bacterial sepsis. Placement of leg wraps and provision of padding adjacent to the foal will minimize trauma.

If the foal is sufficiently medically stabilized and the owner is compliant, transport to a referral facility is possible with the following considerations:

Timeliness. Nothing is worse than a referral too late. Increased costs of treatment to the owner coupled with a decreased prognosis result in a loss to us all as a profession.

Owner financial resources. Hospitalization will be expensive. Complications are provided at no extra cost. Continuous nursing care is expensive but imperative. Ensure secure vascular access; if you place an intravenous catheter ensure that it will remain in place with all attachments. This may be replaced with a longer-term catheter in hospital.

History. Where possible, a written account encompassing treatment to the time of arrival at the hospital. If the responsible person is not coming with the foal, encourage the client to bring your billing/record sheets.

Up to date blood work is imperative. Blood collected before referral will likely be repeated, to establish both a baseline and to gauge response to previous treatments.

Mare compliance. Is it necessary for the mare to accompany the foal? If so, will she adjust to a hospital setting?

Summary

Peripartum hemorrhage in the mare may become a life-threatening emergency depending on the structures involved and the extent of blood loss. Treatment of the mare centers on promoting hemostasis and restoring circulating blood volume in a fashion that does not excessively raise blood pressure and risk restarting hemorrhage. Many established treatments are controversial. The neonatal foal may require resuscitation following delivery as the result of gestational or parturient events. Although many conditions can be managed on the farm, a thorough clinical exam should be performed to identify those foals in need of specialist intervention. Appropriate stabilization and preparation for transport and referral increase the probability of success.

References

1. Wilsher S, Allen WR: Effects of a *Streptococcus equi* infection--mediated nutritional insult during mid-gestation in primiparous Thoroughbred fillies. Part 1: placental and fetal development. Equine Vet J 2006;38:549-557.

2. Ousey JC, Fowden AL, Wilsher S, et al: The effects of maternal health and body condition on the endocrine responses of neonatal foals. Equine Vet J 2008;40:673-679.
3. Dolente BA: Critical peripartum disease in the mare. Vet Clin North Am Equine Pract 2004;20:151-165.
4. Platt H: Caecal rupture in parturient mares. J Comp Pathol 1983;93:343-346.
5. Dart AJ, Pascoe JR, Snyder JR: Mesenteric tears of the descending (small) colon as a postpartum complication in two mares. J Am Vet Med.Assoc 1991;199:1612-1615.
6. Zamos DT, Ford TS, Cohen ND, et al: Segmental ischemic necrosis of the small intestine in two postparturient mares. J Am Vet Med Assoc 1993;202:101-103.
7. Wilkins P: Monitoring the pregnant mare in the ICU. Clin Tech Equine Pract 2003;2:212-219.
8. Rooney J: Internal hemorrhage related to gestation in the mare. Cornell Vet 1964;54:11-17.
9. Dwyer R, Harrison L: Post partum deaths of mares. University of Kentucky Equine disease quarterly 1993;2:5.
10. Dechant JE, Nieto JE, Le Jeune SS: Hemoperitoneum in horses: 67 cases (1989-2004). J AmVet Med Assoc 2006;229:253-258.
11. Pascoe RR: Rupture of the utero-ovarian or middle uterine artery in the mare at or near parturition. Vet Rec 1979;104:77.

12. Arnold CE, Payne M, Thompson JA, et al: Periparturient hemorrhage in mares: 73 cases (1998-2005). J AmVet Med Assoc 2008;232:1345-1351.
13. Gruninger B, Schoon HA, Schoon D, et al: Incidence and morphology of endometrial angiopathies in mares in relationship to age and parity. J Comp Pathol 1998;119:293-309.
14. Stowe HD: Effects of age and impending parturition upon serum copper of thoroughbred mares. J Nutr 1968;95:179-183.
15. Pusterla N, Fecteau ME, Madigan JE, et al: Acute hemoperitoneum in horses: a review of 19 cases (1992-2003). J Vet Intern Med 2005;19:344-347.
16. Heidmann P, Tornquist SJ, Qu A, et al: Laboratory measures of hemostasis and fibrinolysis after intravenous administration of epsilon-aminocaproic acid in clinically normal horses and ponies. Am J Vet Res 2005;66:313-318.
17. Ross J, Dallap BL, Dolente BA, et al: Pharmacokinetics and pharmacodynamics of epsilon-aminocaproic acid in horses. Am J Vet Res 2007;68:1016-1021.
18. Verstraete M. Clinical application of inhibitors of fibrinolysis. Drugs 1985;29:236-261.
19. Gurll NJ, Vargish T, Reynolds DG, et al: Opiate receptors and endorphins in the pathophysiology of hemorrhagic shock. Surgery 1981;89:364-369.
20. Faden AI, Holaday JW: Opiate antagonists: a role in the treatment of hypovolemic shock. Science 1979;205:317-318.
21. Vargish T, Reynolds DG, Gurll NJ, et al: Naloxone reversal of hypovolemic shock in dogs. Circ Shock 1980;7:31-38.

22. Lechner RB, Gurll NJ, Reynolds DG: Effects of naloxone on regional blood flow distribution in canine hemorrhagic shock. Proc Soc Exp Biol Med 1985;178:227-233.

23. Weld JM, Kamerling SG, Combie JD, et al: The effects of naloxone on endotoxic and hemorrhagic shock in horses. Res Commun Chem Pathol Pharmacol 1984;44:227-238.

24. Ferguson JL, Roesel OF, Bottoms GD: Dexamethasone treatment during hemorrhagic shock: blood pressure, tissue perfusion, and plasma enzymes. Am J Vet Res 1978;39:817-824.

25. Hellman A, Haggendal E, Lundberg D: Hemodynamic effects of massive doses of dexamethasone in controlled hypovolemic shock in the dog. Acta Anaesthesiol Scand 1982;26:222-224.

26. Pfueller SL, Hosseinzadeh P, Firkin BG, et al: Activation of platelet coagulant activities by formalin. Thromb Haemost 1978;39:546-548.

27. Taylor EL, Sellon DC, Wardrop KJ, et al: Effects of intravenous administration of formaldehyde on platelet and coagulation variables in healthy horses. Am J Vet Res 2000;61:1191-1196.

28. Ali M, Abdus S: Comparative studies on systemic coagulants in ruminants. Indian Vet J 1973;50:27-31.

29. Graham L, Farnsworth K, Cary J: The effect of yunnan baiyao on the template bleeding time and activated clotting time in healthy halothane anesthetized ponies. Proc Int'l Vet Emergency Crit Care Soc 2002. p. 790.

30. Marroum PJ, Webb AI, Aeschbacher G, et al: Pharmacokinetics and pharmacodynamics of acepromazine in horses. Am J Vet Res 1994;55:1428-1433.

31. Ballard S, Shults T, Kownacki AA, et al: The pharmacokinetics, pharmacological responses and behavioral effects of acepromazine in the horse. J Vet Pharmacol Ther 1982;5:21-31.

32. Magdesian KG, Fielding CL, Rhodes DM, et al: Changes in central venous pressure and blood lactate concentration in response to acute blood loss in horses. J Am Vet Med Assoc 2006;229:1458-1462.

33. Hurcombe SD, Mudge MC, Hinchcliff KW: Clinical and clinicopathologic variables in adult horses receiving blood transfusions: 31 cases (1999-2005). J Am Vet Med Assoc 2007;231:267-274.

34. Nolan J: Fluid resuscitation for the trauma patient. Resuscitation 2001;48:57-69.

35. Dubick MA, Atkins JL: Small-volume fluid resuscitation for the far-forward combat environment: current concepts. J Trauma 2003;54:S43-S45.

36. Dubick MA, Bruttig SP, Wade CE: Issues of concern regarding the use of hypertonic/hyperoncotic fluid resuscitation of hemorrhagic hypotension. Shock 2006;25:321-328.

37. Knutson JE, Deering JA, Hall FW, et al: Does intraoperative hetastarch administration increase blood loss and transfusion requirements after cardiac surgery? Anesthesia Analgesia 2000;90:801-807.

38. McCleane G: Intravenous lidocaine: an outdated or underutilized treatment for pain? J Palliat Med 2007;10:798-805.

39. Doherty TJ, Frazier DL: Effect of intravenous lidocaine on halothane minimum alveolar concentration in ponies. Equine Vet J 1998;30:300-303.

Table 1: Useful drug dosages for the postpartum mare

Sedation:

Care should always be exercised in the administration of sedation to the pregnant mare. Most agents cause hypotension which will exacerbate the negative effects of hypovolemia.

Xylazine: 0.25 to 1 mg/kg iv or im. Potent hypotensive effects.

Detomidine: 0.01 to 0.02 mg/kg iv or im. Less hypotensive potential than xylazine.

Butorphanol: 0.01 to 0.02 mg/kg iv or im. Give as needed, may be repeated every 8 to 12 h. Effects will be attenuated where naloxone is administered concurrently.

Acepromazine: 0.02 mg/kg im q 12h. Potent hypotensive agent, use with caution.

Analgesia:

Flunixin: 1 mg/kg iv q 12h

Lidocaine: load with 1.3 mg/kg slow iv bolus of lidocaine 20% followed by 0.05 mg/kg/min iv as a constant rate infusion. May be conveniently made by adding 450 ml lidocaine 20% to a 3 L fluid bag and administering at 1 ml/kg/h.

Hemostatic agents:

ε-aminocaproic acid: 40 mg/kg iv load then 20 mg/kg iv q 6-8h. Administer in 1 L fluids over 15-30 min. Five or more doses may be required if hemorrhage ongoing.

Yunnan baiyao: 8 mg/kg po q 6h. Administer 16 x 0.25g capsules in water as paste q 6h. Duration of treatment is highly variable, being 2 to 4 d.

Circulatory support:

Naloxone: 0.01 to 0.02 mg/kg iv. Administered in initial treatment phase, may be repeated.

Polyionic fluids: 2 ml/kg/h iv (maintenance rate). Continued throughout the period when fluid intake by other means deemed inadequate.

Hypertonic saline: 2 to 4 ml/kg iv. Controversial due to potential for a rapid rise in blood pressure. Given during the initial fluid resuscitation period.

Hetastarch: 6 to 10 ml/kg iv. Administered during the initial fluid volume restoration period only.

Table 2: Useful drug dosages for the foal.

Antimicrobials:

Duration of treatment is governed by clinical response. A minimum of five d should be administered in the absence of adverse reactions.

K penicillin: 40000 to 50000 units/kg iv q 6h

Ceftiofur sodium: 2 mg/kg im q 12h or 5 to 10 mg/kg iv q 6-12h

Amikacin: 25 mg/kg iv q 24h

Trimethoprim-sulfamethoxazole: 30 mg/kg po bid

Seizure control and metabolic support:

Diazepam 0.05 to 0.4 mg/kg iv. Short-acting control following acute onset of seizure activity. May repeat 2 to 3 times as required to establish control.

Phenobarbital 4 to 10 mg/kg iv. Long-acting control useful when initial agent fails. May be repeated at 12 h intervals for continued control, or change to oral phenobarbital at 4 mg/kg po q 12h.

Thiamine 10 mg/kg iv q 24h. Cerebral metabolic support. Useful in initial stages of hypoxic insult.

Control cerebral edema and inflammation:

Hypertonic saline 7 ml/kg iv as 3% solution. Shown to aid in control of cerebral edema. Useful in initial period following insult.

Mannitol 1 mg/kg iv as 20% solution. May repeat at 12 h intervals until appropriate mentation returns, often 2 to 3 d sufficient.

Flunixin meglumine: 1 mg/kg iv q 12h. Continue while clinical signs evident.

Ketoprofen: 2 mg/kg iv q 24h. As for flunixin. Less ulcerogenic potential.

Control oxidative damage:

Vitamin C 100 mg/kg iv q 24h. Useful in the initial stages following onset of cerebral compromise. Three d treatment or more may be required and this is safely administered.

Vitamin E 20 iu/kg sc q 24h. Requires prolonged administration to reach therapeutic levels in central nervous system.

Dimethyl sulfoxide 1 g/kg iv q 12h as 10% solution. Useful during period when ongoing damage is suspected to be occurring, often up to three d post insult.

Respiratory stimulant

Caffeine 10 mg/kg po load, then 2.5 mg/kg po q 6h. Continue until appropriate respiratory pattern is established. May cause hyperactivity and lower the seizure threshold in some foals.

Table 3: Resuscitation protocol for the compromised neonate.

Airway

- Intubate by nasotracheal route with largest practical endotracheal tube
- Extend neck and twist as arytenoids reached to ease passing
- Size **8 to 10 mm** suitable for average foals
- Pass tube to nares to minimize dead space
- Compress chest and palpate esophagus to ensure correct placement

Breathing

- Respiratory arrest usually precedes cardiac arrest in the neonatal foal
- Establish rate of **8 to 10** breaths/minute with 1 second inspiration period
- Use 100% oxygen if available, however room air is acceptable
- The use of a self-inflating resuscitation bag with a pressure limiting valve (**Ambu**), or any other similar delivery device, will aid ventilation and avoid excessive inflation pressure
- **Doxapram** (controversial) at **0.5 mg/kg** iv

Circulation

- Thoracic compressions if **HR less than 60**, especially if less than 60 and not increasing
- Minimize interruptions (no longer than 10 seconds)
- Rapid compressions (aim for **100/minute**)
- Establish vascular access if response is not immediately favorable

Drugs

- Usage and rationale based on experience and extrapolation
- Heart rate **less than 60 and not increasing**
- Continue compressions to distribute drugs
- **Epinephrine** at **0.02 mg/kg** (0.5 to 1 ml of 1:1000 per 50 kg foal). Intratracheal dose 5 to 10x this, however absorption is poor
- Repeat every 3 to 5 minutes until response is noted
- Administer **10 ml/kg** of a balanced electrolyte solution. A 2 to 4 ml/kg hetastarch bolus may be useful to rapidly expand circulating volume
- Avoid inducing hyperglycemia with dextrose containing solutions as resulting hyperinsulinemia is depressive
- **Dobutamine** at **3 to 40 μg/kg/min** iv is useful to improve pulse pressure and peripheral perfusion

Everything else

- Monitor foal progress
- Pupillary light responses: dilated pupils indicate lack of cerebral perfusion
- Stop when HR above 60 (pause 10 seconds max)
- Spontaneous breathing (pause 30 seconds)
- End point determination

Table 4: Times of importance to the neonatal foal.

- Sternal Recumbency: the foal should right itself and be able to remain sternal within 5 to 10 minutes of birth.
- Standing: within 60 minutes (range of 15 to 165 minutes). Compromised neonates tend to remain recumbent longer, further exposing themselves to pathogens.
- Suckle reflex: usually develops within 20 minutes of birth, although may be much sooner.
- Suckling: the foal should suckle the mare within 2 h (range 35 minutes to 7 h).
- Urination: first urination occurs at 6 h for colts, 10 h for fillies.
- Urine production: approximately 6 mL/kg/hr. Decreases may result from decreased fluid intake, increased losses or compromises in renal function. Obstruction or disruption due to rupture and uroperitoneum are possible in the compromised neonate, or one which sustained trauma during parturition.
- Defecation: foals display abdominal straining within the first few h after of birth, and pass meconium completely within 24 h. Colostrum stimulates GI motility. Any interference with GI motility will prolong passage of meconium increasing the likelihood of impaction.

Table 5: Examination of the neonatal foal.

- Rectal temperature

  Appropriate neonatal range 99 °F to 101.5 ºF. Neonatal foals are unable to regulate body temperature to the same degree as older foals.

- Cardiovascular system

  Appropriate neonatal heart rate (HR) range is between 70 to 120 beats per minute. HR is highly labile, however rate and rhythm is regular. Pulses are synchronous with the heart beat and easily palpable. Deviations may indicate arrhythmia (electrolyte abnormality, congenital cardiac anomaly). A murmur associated with a PDA can occur for the first few days of life.

- Respiratory system

  Within the first hour of life, the respiratory rate (RR) of a normal foal can rise up to 80 breaths per minute. The RR decreases progressively over the next few days, with a subsequent range of 30 to 40 breaths per minute. Increased RR may indicate compromised pulmonary function, pain, excitement or fever. The magnitude of the thoracic excursion is indicative of the respiratory effort. Any decrease may indicate fatigue. Nostril flaring may be the only indication of increased respiratory effort.

- Musculoskeletal system

Joint distension: indicative of sepsis, coagulopathy (hemarthrosis), trauma.

- Integument

  Decubital ulcers indicate trauma, unseen seizure activity or the occurrence of prolonged recumbency. Pitting edema suggests hypoproteinemia or cardiac dysfunction. Icterus suggests sepsis, neonatal isoerythrolysis, or hepatic disease. Hemorrhage on the mucous membranes suggests sepsis, coagulopathy or direct trauma.

- GI function

  Any occurrence of colic has the potential to indicate a life-threatening episode and should be thoroughly investigated.

- Urinary function

  Acute renal failure may occur as the result of decreased *in utero* blood supply or be iatrogenic from nephrotoxic drug usage. Uroperitoneum results from a ruptured bladder, ruptured urachus or torn ureter.

- Ocular examination

  Hyperemia of the sclera indicates birth trauma, sepsis, or coagulopathy.

  Entropion results from weight loss or dehydration leading to enophthalmia.

  Corneal opacity is the result of ulceration, a depressed blink response, lack of tear production, or exposure keratitis in the depressed neonate.

Anterior chamber: can reflect systemic inflammation and sepsis. Fibrin deposition (aqueous flare) and hypopyon may result.

- Mentation and nervous function

  Hypoxic ischemic encephalopathy causes loss of affinity for the mare, generalized depression and a lack of vigorous suckling. Low level seizure activity may appear as muscle fasciculations, chewing fits, or unexplained cutaneous trauma. The menace response is absent from the neonate and is not an indication of vision. This reflex will take between 4 to 14 d to develop.

HEMATOLOGY

- Normal neonatal range (birth to 1 week): RBC range from 7.4 to 11.4 million cells/uL. WBC range from 4.9 to 13.6 thousand cells/uL.
- Neutrophils (N): approximately 5500 cells/µL are present at birth with this increasing to 8000/µL within the first 12 h of life.
- Lymphocytes (L): may decrease to approximately 1400 cells/µL within a few hours of birth, thereafter they increase to approximately 5000 cells/µL by 3 months of age. A transient decrease to below 1000 cells/µL may occur in some normal foals, but this may also indicate infection or immune compromise.

SERUM CHEMISTRY

In the absence of established foal parameters in many laboratories, normal adult equine values are often used for assessment of neonatal foal health.

- Serum electrolyte concentrations are maintained within a narrow range and do not differ substantially from established adult values.
- Glucose is elevated compared to adults due to frequent suckling. Hypoglycemia is cause for concern as this may indicate of sepsis or decreased feeding activity.
- Plasma protein levels at birth vary considerably between foals.
- Serum creatinine and BUN are unreliable indicators of newborn foal renal performance as the placenta is primarily responsible for elimination of waste products; therefore an increase reflects placental dysfunction. However, BUN and creatinine may be initially elevated decreasing to adult levels by 3 to 5 d.
- Total bilirubin may be elevated as mild icterus is common. Consider sepsis, isoerythrolysis or hepatic disease.
- Creatine kinase is raised by muscle trauma from delivery.
- Alkaline phophatase is elevated due to rapid growth in the neonate.
- GGT elevations may be of colostral origin.
- Fibrinogen is uniformly low in the healthy neonate (up to 200mg/dL). Elevated levels indicate *in utero* challenge with prenatal response.
- IgG concentration: there is a strong association between the occurrence of sepsis and an immunoglobulin concentration less than 400mg/dL. Catabolism of immunoglobulins may occur in the compromised neonate.