Prevention and Outbreak Management of Foal Diarrhea

Nathan M. Slovis DVM, Dipl. ACVIM, CHT
Lexington, KY

Gastrointestinal disease is associated with a variety of disorders in foals. Failure of this organ system may manifest as diarrhea, ileus, abdominal pain, obstipation and weight loss. Clinical syndromes associated with gastrointestinal failure include enteritis, colic, meconium impactions, gastric reflux and necrotizing enterocolitis. The following will review the pathogenesis, clinical manifestation, diagnosis and treatments for the aforementioned syndromes of gastrointestinal failure.

ENTERITIS

Diarrhea is among the most common clinical complaints in foals. According to the National Animal Health Monitoring System equine '98 study, diarrhea affected > 20% of foals within the first 6 months of age. Although diarrhea is common with enteritis (inflammation of the small intestine), diarrhea is not always associated with inflammation of the bowel. Before the veterinarian can consider a treatment course for diarrhea they must understand the mechanisms of diarrhea. Is it malabsorptive or secreterory diarrhea? Is it infectious or non-infectious? Malabsorptive is the inability of the intestinal tract to reabsorb water and nutrients. Secretory diarrhea results in the hypersecretion of both water and electrolytes into the intestinal tract. In a general categorization, bacterial toxins (Ex. Salmonella or Clostridium spp.) may cause a secretory diarrhea while viruses (Ex. Rotavirus and Coronavirus) can result in a malabsorptive diarrhea. In severe infections both bacteria and viruses can result in both a secretory and malabsorptive diarrhea. Most infectious causes of diarrhea and enteritis result in signs of mild to severe abdominal pain.

Diagnosing the cause of enteritis in foals can be difficult because of the myriad of potential causes. Obtaining historical information can provide clues to the etiology of the enteritis. Questions may include:

- Have there been or currently any other animals on the farm having fevers or diarrhea?
- Has the foal received any medications that may have predisposed it to gastrointestinal disease?
- Have there been any changes in management (Feeding, turnout and etc.)?
- What is the consistency of the feces? Fetid in odor?
- What is the age of the foal?

The most common life-threatening problem associated with enteritis is hypovolemic or septic shock. Hypovolemic shock is characterized by pale mucus membranes, prolonged capillary refill time and rapid weak pulses. Septic shock is commonly recognized by hyperemic mucus membranes, rapid capillary refill time and bounding/hyperdynamic pulses. The physical parameters of shock vary as a continuum with the stage of shock. Aggressive fluid therapy is the initial treatment for hypovolemic or septic shock. Blood samples should be obtained for pretreatment evaluation involving complete blood cell count (CBC), serum chemistry profile and ionized calcium. Lactate levels (Normal <2.5mmol/l in a recumbent foal) can also be monitored to evaluate potential hemodynamic disturbances. Electrolyte disturbances are common during enteritis. Hyponatremia, hypochloremia and metabolic acidosis are common findings.

Ultrasonography is very helpful in distinguishing between small and large intestinal disease and when considered with blood results can also help determine medical versus surgical lesions.

The stomach in the normal foal can be visualized in the 9-13th intercostal spaces on the left side medial to the spleen. Normally it is recognizable as a white curvilinear area adjacent to the spleen at the level of the splenic vein. When distended it's dimensions can extend beyond the last rib and a greater portion of the left side. With severe distention the stomach can also be
noted along the ventral abdomen extending across the midline to the right side. As the stomach becomes distended because of ileus and reflux, the duodenum and jejunal segments are likely to also be dilated and fluid distended. The duodenum is imaged on the right side starting at the caudal pole of the right kidney in the paralumbar fossa, where it can be visualized, situated between the kidney dorsally and the cecal base ventrally. The duodenum courses cranially to about the level of the 11th intercostal space on the right side. The jejunum may not be able to be easily visible, but when distended this portion of the small intestine is easily recognized.

Ultrasonographic findings in the proximal enteritis patient will usually include gastric, duodenal and small intestinal distention. Relief of gastric distention following decompression will quiet the animal down whereas pain from a strangulating lesion will be expected to cause unremitting pain.

Infectious causes of gastrointestinal disease in neonates may include Rotavirus, Coronavirus, Clostridium perfringens A and C, Clostridium difficile, Camplobacter, Enterococcus durans, Bacteroides fragilis and Rhodococcus equi.

Non-infectious causes of gastrointestinal disease include hypoxic ischemic necrotizing enterocolitis, foal heat diarrhea, diet and ingestion of sand.

INFECTIOUS

Rotavirus

Foals are most susceptible to viral diarrheas during the neonatal, perinatal and suckling periods by virtue of being immunological naïve. Clinical signs of disease have been reported only among foals < 6 months old and most often among foals < 3 months old. Signs include diarrhea, lethargy, anorexia and abdominal tympani. A 3-year study of horse farms in central Kentucky during the 80's noted that rotavirus was the most common cause of diarrhea in foals.

Rotavirus is species specific with an incubation period of 1-2 days. The virus invades the intestinal epithelium on the sides and the tips of the villi. The brush border epithelium of the small intestine synthesizes disaccharides to monosaccharides (glucose and galactose), which are absorbed in the gut. Destruction of the brush border villi results in decreased lactase formation, which results in lactose not being digested. This sugar remains in the lumen of the gut, osmotically attracting more fluid. This effect is compounded as bacteria in the large intestine ferment the lactose into acetate, propionate and butyrate, which increase osmolality of the colonic contents.

Foals infected with rotavirus may shed the virus for up to 10 days. Some horses may shed the virus for up to 8 months. The virus can persist in the environment for up to 9 months. Diagnosis requires detection of the virus in feces. The tests include electron microscopy, enzyme linked immunoassay (ELISA), Polymerase chain reaction (PCR) and latex agglutination virogen rotatest. In a recent study by the author it was noted that when comparing the human specific rotavirus antigen detection (Rotatest) with an equine specific real-time PCR (IDEXX Equine Diarrhea Panel RealPCR ™) we uncovered the inadequacy of using some human diagnostic tests in veterinary medicine (false negatives).

Treatments are generally empirical and symptomatic including precautionary antibiotics and anti-ulcer medications (Carafate 1 gram per 50kg Body Weigt PO QID and/or Omeprazole 1-4mg/kg PO SID). Lactase 6,000 food chemical codex (FCC) lactase U / 50kg PO Q 3-8 hours for 10-14 days have been used to improve digestion of milk lactose. Antidiarrheal medications such as bismuth subsalicylate (1-3ml/kg PO SID to QID) may help reduce bowel inflammation and provide for secondary toxin absorption and resorption when combined with activated charcoal (1gram/kg SID). Neostigmine (1mg SQ Q 1hr to 8 hr (IV if severe tympany) is often used to help relieve gastrointestinal tympany. Fluid therapy is necessary to correct hydration, shock and electrolyte imbalances. Prevention of this disease includes proper hygiene and the use of phenol disinfectants because bleach is ineffective against this virus. A commercial modified live vaccine...
is currently available for use in mares prior to foaling to help accentuate colostral antibodies. It has been noted that foals from vaccinated mares can still become infected with rotavirus although the clinical signs may be attenuated. One novel treatment plan currently used as an adjunctive treatments for both viral and bacterial causes of diarrhea is the use of Bentonite clay. Not all bentonite clay is created equally and currently there is a ultra-purified bentonite clay that is available for use in our equine patients.

**Coronavirus**

Equine coronavirus was isolated and characterized only recently in 2000 but described as infectious agent in sick foals in 1976. Several studies and case reports have identified coronaviruses in foals with enteric disease but the pathogenicity and its etiologic role in enteric disease have not been examined. A recent prevalence study in Central Kentucky by the author clearly shows that healthy foals without signs of GI disease are equally infected with equine coronavirus as sick animals. This finding suggests low pathogenicity of ECoV in foals. However, when analyzed as coinfecting agent, ECoV was significantly associated with diseased animals: all ECoV infections in the GI diseased group were associated with coinfections (15 of 15) while foals in the healthy group were mostly monoinfected (8 of 10). This finding would support the theory that (certain) viruses primarily act as immune suppressing agents allowing opportunistic infections to take place. Opportunistic infections can be of different origin, including bacterial or protozoal, as shown in this study. Coinfection data in piglets clearly indicate that coronavirus and bacterial coinfections have a significant effect on the magnitude of the inflammatory immune response and the amount of tissue damage compared to single infected animals. Furthermore, in young turkeys, coronavirus and enteropathogenic *Escherichia coli* (EPEC) were shown to synergistically interact and cause severe growth depression and high mortality when compared to monoinfected turkeys. In this study, turkeys infected first with coronavirus and then with EPEC developed numerically greater mortality, significantly lower survival probability, and increased frequency of attaching and effacing lesions than that observed in turkeys inoculated with EPEC prior to turkey coronavirus or simultaneously inoculated with these agents; these observations not only suggest a role for coronavirus in foals, it also suggests diagnostic value of detecting ECoV in apparently healthy foals to assess their susceptibility for potentially detrimental coinfections. In coronavirus infected healthy foals the focus could be directed towards epidemiological aspects in order to reduce the likelihood of coinfections. Clearly, additional studies are needed to determine equine coronavirus virulence factors and the relative importance as a coinfecting agent to contribute to GI disease in foals.

**Diagnosis:** Polymerase chain reaction, Virus isolation or electron microscopy. **Treatment:** Refer to Rotavirus. Currently there is a ultra-purified Bentonite clay that is available for the use in horses that has the same composition as a product being investigated in humans suffering from Rotavirus or Coronavirus gastrointestinal infections.

**Clostridium difficile**

*Clostridium difficile* is the agent that causes pseudomembranous colitis associated with antibiotics in humans. It is now being identified in recent years as a significant nosocomial pathogen for equine as well as human patients. First described in 1935 by Hall and O'Toole, this gram-positive anaerobic bacillus was named “the difficult clostridium” because it resisted early attempt at isolation and grew very slow. The organisms were found in stool specimens from healthy human neonates (up to 50%) which, led to its classification as a commensal and was subsequently ignored as a potential pathogen. In the 1960’s and 1970’s antibiotic-associated pseudomembranous colitis became a major clinical problem, which was attributed to mucosal ischemia or viral infection. In 1977, Larson et al. reported that stool specimens from affected patients contained a toxin that produced cytopathic changes in tissue culture cells. *C. difficile* was identified as the source of the cytotoxin. It is now clear that *C. difficile* is responsible for virtually all cases of human pseudomembranous colitis and 20% of the cases of antibiotic induced colitis.

**Pathogenesis** of antibiotic-associated diarrhea/colitis begins with a disruption of colonization resistance (disruption of the normal colonic flora) of *C. difficile*. Colonization occurs by the oral-
clostridial strains. Differentiation of toxigenic strains from nontoxigenic strains is particularly important because they can bind to the toxins. PCR techniques can also be used to detect these toxins in fecal samples which were refrigerated at 4°C for 60 days. 18

Strains that do not produce toxins are not pathogenic. Two large exotoxins, toxin A (enterotoxin) and toxin B (cytotoxin) are produced by Clostridium difficile. These toxins have been validated for use in feces of horses. 18

When established in the colon, pathogenic strains of Clostridium difficile produce toxins that cause diarrhea and colitis. Strains that do not produce toxins are not pathogenic. Two large exotoxins, toxin A (enterotoxin) and toxin B (cytotoxin) are produced by Clostridium difficile. Toxins A and B appear to act synergistically which cause fluid secretion, mucosal damage, and intestinal inflammation. Recent studies have demonstrated that neither Clostridium difficile or cytotoxin B was found in the fecal flora of 56 healthy foals (14 days to 4 months of age) not being treated with antibiotics. 21 Similarly, a small percentage of foals are reported to be asymptomatic carriers with reported ranges from 0-3%. Reported rates of asymptomatic carriers in adult horses are very similar to that of humans (< 1 to 15% of healthy adults) range from 0 to 4%. 21 This organism, therefore is most likely a minor and uncommon component of the usual gastrointestinal tract flora. Diarrhea and fatal hemorrhagic necrotizing enterocolitis have been reported to occur in neonatal foals infected with toxigenic strains of Clostridium difficile, and Clostridium difficile may be a primary pathogen in foals, not requiring prior antimicrobial use for development of the disease. 21

Clinical presentation of Clostridium difficile in foals range from low-grade diarrhea to fulminate colitis with ileus. The foals with severe colitis become anorexic and dehydrated. In addition to the diarrhea, foals become tachytpnea, which may be, secondary to discomfort associated with the enteritis, pyrexia, metabolic acidosis or the anxiety of being in the hospital. Hyponatremia is also a feature of Clostridium difficile secondary to the effects of toxins A and B leading to extravasation of plasma proteins. Metabolic acidosis is also consistent with clostridial enterocolitis and hypovolemia or gastrointestinal tract loss of bicarbonate. Hyponatremia may also be attributable to the gastrointestinal tract losses, as well as to an excess of free water associated with water consumption by these foals.

Diagnosis of Clostridium difficile infection depends on the demonstration of Clostridium difficile toxins in the stool. The cytotoxin assay that uses tissue culture cell culture had been the gold standard for diagnosis. It is the most sensitive test (sensitivity 94-100% and specificity 90%), detecting as little as 10 pg of toxin B (This test is not used commonly because it is time consuming and expensive). A stool culture of Clostridium difficile is a less efficient method of establishing a laboratory diagnosis, since some strains of Clostridium difficile are nontoxicogenic (approximately 25%). More recently, 2 new enzyme immunoassays have been introduced that 1) detect toxin A/toxin B (Clostridium difficile TOX A/B test, Techlab®, Blacksburg VA USA ) or 2) detect antigen of Clostridium difficile and toxin A (TRIAGE Micro; BIOSITE, San Diego CA 1-888-BIOSITE). These tests have a good sensitivity (69-87%) and specificity (99 to 100%). Clostridium difficile TOX A/B test, Techlab® has been validated for use in feces of horses. 24 The Clostridium difficile toxins have been found to be stable in fecal samples which were refrigerated at 4°C for 60 days. 25 DO NOT USE STYROFOAM CUPS to submit a fecal sample because they can bind the toxins. PCR techniques can also be used to differentiate toxicogenic strains from nontoxicogenic strains in feces or among bacterial isolates.
However, PCR methods can detect toxigenic *Clostridium difficile* organisms that are present in low and clinically irrelevant levels.  

**Treatment** in managing diarrhea and colitis with confirmed or suspected *Clostridium difficile* infection is to discontinue antibiotic therapy, if possible. Specific therapy is aimed at eradicating *C. difficile* from the intestinal tract. Oral metronidazole is the drug of first choice. Adult horses are dosed at 15mg/kg PO TID-QID and foals less than 6 months of age are dosed at 10-15mg/kg BID-TID. The response rate for *C. difficile* in patients (humans) taking metronidazole is 98%. Patients who can not tolerate oral medication because of an ileus may either receive the same dose per rectum or can be effectively treated with intravenous metronidazole at 10mg/kg TID to QID. Excretion of the drug into bile and exudation from the inflamed colon results in bactericidal levels in the feces.\(^{26}\) Metronidazole resistant strains of *C. difficile* have been isolated, and there are even reports of metronidazole inducing colitis. For resistant strains of *C. difficile* the use of vancomycin orally is indicated. The dose is 4mg/kg PO loading dose then 2mg/kg PO Q6h. When oral vancomycin is prescribed I recommend the use of the parenteral solution because of the expense. It is recommend that treatment be continued for 5 days past the resolution date of the diarrhea. A substantial number of human patients 10 to 20% will have a relapse of *C. difficile* diarrhea. Various other approaches have been suggested for the management of relapses, including slow tapering of metronidazole therapy, bacteriotherapy with the use of nasogastric fecal transfaunation or fecal enemas, oral administration of nontoxicogenic *C. difficile*, and treatment with the yeast *Saccharomyces boulardii* (may compete with *C. difficile* toxin A for binding sites on the intestinal epithelium).\(^{26}\) *Saccharomyces boulardii* anecdotally can be given to a foal at dose rate of 5 billion colony-forming units orally 2x a day. One novel treatment plan currently used as an adjunctive treatments for both viral and bacterial causes of diarrhea is the use of Bentonite clay. Bentonite is effective because it bonds to a variety of toxins and prevents the absorption of toxins by coating the intestinal wall.\(^{27}\) Not all bentonite clay is created equally and currently there is a ultra-purified bentonite clay that is available for use in our equine patients.\(^{9}\) There is a hyperimmunized *Clostridium difficile* Toxin a and B plasma that is currently available.\(^{6}\) The efficacy of the plasma in resolving diarrhea/toxic insult is currently anecdotal.

**Clostridium perfringens**

*Clostridium perfringens* is a relative ubiquitous bacterium that has been associated with enteric diseases in a number of diverse species.\(^{28}\) It is wide spread in the soil and is found in the alimentary tract of nearly all warm-blooded species. *Clostridium perfringens* is a frequent postmortem invader in the alimentary tract’s tissues of bloating cadavers. Therefore, one must be cautious about drawing conclusions based on the presence of the organisms in the tissues of these animals. Types of *C. perfringens* are differentiated (5 major types A, B, C, D and E) based on the production of 4 major toxins; alpha, beta, epsilon and iota. In addition isolates may have the gene known as *C. perfringens* enterotoxin (CPE). It is produced by sporulating cells in an alkaline environment and is released upon LYSIS of these cells. It is resistant to proteolytic enzymes and will bind and insert on the brush border membrane causing pore formation in cells leading ultimately to cell lysis. Enterotoxin can be produced by all types of *Clostridium perfringens* but is most commonly associated with type A. Many factors are involved in the production of enterotoxin by *C. perfringens*. In one study the prevalence of CPE in feces of adult horses with diarrhea was 16% and detected in only 10% of the horses with colic regardless of whether or not they had diarrhea.\(^{29}\) Studies investigating CPE in feces of adult horses and foals with diarrhea have produced variable results. CPE has been detected in the feces of 7% to 33% of adult horses with diarrhea and 28% of the foals with diarrhea.\(^{28\text{-}30}\) Furthermore, out of 843 *C. perfringens* type A isolates from dogs, people, and horses that were genotyped only 62 (7.3%) contained the CPE gene.\(^{30}\)

Recently an unassigned type of *C. perfringens* that produces alpha-toxin and the newly discovered β2-toxin was described.\(^{31}\) It was isolated from piglets with necrotic enterocolitis and was also found in horses with enterocolitis. Since the alpha toxin, which is produced by all types of *C. perfringens* including non-pathogenic type A strains, is not considered a primary cause of digestive lesions; it was suggested that the β2-toxin, which is present in this new type of C.
**perfringens**, is responsible for the lesions. In a recent study they found that β2-toxin was found in 52% of the horses with typical and atypical typhlocolitis. To a lesser extent they were also isolated from horses with other intestinal disorders, in which they represented 37% of the isolates. No β2-toxinigenic *C. perfringens* has been found in healthy horses or in horses hospitalized for reasons other than intestinal problems.\textsuperscript{31}

**Pathogenesis** of *C. perfringens* is based on their production of one or more of the 4 major exotoxins or enterotoxin. The factors that lead to the development of disease are not clear, but it is believed that there is an alteration of the normal flora that allows overgrowth of the clostridia. Proposed causes include diet changes, antibiotic therapy, stress, or concurrent infection. In adult ponies, enterocolitis has been produced when antibiotics (clindamycin or lincomycin) were given to the animals orally with a fecal cocktail containing clostridium.\textsuperscript{32} However, fecal cocktail alone did not cause disease. Other factors that may play a role in the development are host factors such as age, immunity, and the presence or absence of intestinal receptors for the perfringens toxins. Beta toxin-producing types of *C. perfringens* (Type C) appear to cause enterocolitis in neonatal animals only. The digestive enzyme trypsin is produced by older animals and can inactivate the toxin. Neonatal animals have a less developed digestive enzyme production, thus may be more susceptible to disease caused by this toxin.\textsuperscript{32} Most of the affected foals in one study had serum IgG concentrations of >800mg/dl, indicating adequate passive transfer. This finding helps support a theory that trypsin inhibitor in the dam’s colostrum, which protects immunoglobulins from gastrointestinal breakdown, may potentially allow *C. perfringens* type C β-toxin to persist in foals with adequate passive transfer and may allow type C bacteria to overgrow.

**Clinical appearance** of the disease is usually associated with foals < 5 days of age with a history of being obtunded, colicky and/or diarrhea for less than 24 hours. The animals usually present dehydrated with a severe colitis. Some of the animals may develop an ileus with evidence of colonic distention. Clinical pathology work-up for a majority of these cases reveals that the animal is acidotic (HCO3 10-15 Meq/L), azotemic and occasionally hypoglycemic. The complete white blood cell count is characterized as a leukopenia with a toxic left shift. Some of these animals may develop a protein losing colitis secondary to severe intestinal inflammation.

**Specific diagnosis** and definitive diagnosis of equine clostridial enterocolitis requires both identification of toxins and isolation of the organism from intestinal contents. Isolation of the organism without the analysis for toxins is considered inappropriate because of the possibility of isolating a non-enterotoxinogenic *C. perfringens* type A which can be isolated from normal horses' manure. In a population study of fecal shedding of *C. perfringens* in 128 broodmares and foals *C. perfringens* was isolated from 90% of the normal 3-day old foals. 85% were identified as type A; 12% of the samples had type A with the β2-toxin gene isolated. *C. perfringens* with the enterotoxin gene was identified in 2.1 % of samples and *C. perfringens* type C was identified in < 1 % of the samples. A presumptive diagnosis may be made (until culture and toxin analysis) by demonstration of abundant gram-positive bacteria in a fecal smear. However this test did not appear to be sensitive because *C. perfringens* was isolated from 59% of samples in which no gram-positive rods were seen.\textsuperscript{33} The diagnosis is supported by culture of fecal clostridia and further verify the isolates as *C. perfringens* by the use of a polymerase chain reaction method that incorporated primers that allowed for classification of *C. perfringens* types A, B, C, D and E, as well as genes for β2-toxin and enterotoxin (CPE). However, toxin detection kits are commercially available for identification of *C. perfringens* enterotoxin (*C. perfringens* enterotoxin test, ELISA, Techlab®, Blacksburg, VA USA).

**Treatment** for neonatal *C. perfringens* is considered a medical emergency. Even with the best care, many foals can die if infected with *C. perfringens* type C. Neonates with clostridiosis are at a higher risk for the development of peritonitis. When there is a large volume of peritoneal exudate, the prognosis is grave and euthanasia would be recommended. If attempted the treatment plan should be aggressive and aimed at the following areas: abdominal pain, septic shock, clostridial infection and toxin production and maintenance of nutrition. The use of oral metronidazole 10-15mg/kg 3-4x daily (dose depends on severity) for foals and 15mg/kg 3-4x daily for adults. If the animal has an ileus and is intolerant of oral feeding then the use of intravenous metronidazole is recommended at a dose of 10mg/kg IV 4x daily. Should the foal develop an ileus with marked colonic distention we have used neostigmine 1-2mg (2mg for foals greater than 250 pounds) SQ with good clinical response. The author will administer 2-3 doses at 1-hour
intervals and then use it as needed. Oral and IV administration of *C. perfringens type A*, *C and D* hyperimmunized plasma may be given to the neonate. The oral dosage would range from 50-100cc every 6 hours for 48-72 hours. If the animal is severely ill the author would nasogastrically intubate the foal with 250-500ml of the hyperimmunized plasma. So far subjectively, foals given the hyperimmunized plasma appeared to have their manure become formed faster than the patients not treated with the plasma. Bentonite clay can also be used for treatment since it has been shown to adsorb *Clostridium perfringens* alpha, beta and beta-2 exotoxins without interfering with absorption equine collostral antibodies.

Numerous prophylactic measures can be instituted on farms with a history of *C. perfringens*-associated enterocolitis in foals. Optimal hygiene efforts to ensure cleanliness of the foaling stall and the mare (clean udder before and after birth, clean the perineal and hind limb region) at parturition should be undertaken to decrease the degree of exposure of the foal to pathogens in the feces. Some farms have stopped their outbreak of foal diarrhea by foaling the mares out in pasture. Oral administration of lactobacillus acidophilus (found in yogurt and commercial probiotics) have been successfully used in chickens to minimize the overgrowth of *C. perfringens*. Prophylactic use of metronidazole (10mg/kg PO BID) has also been instituted after birth. In mares that have a good history of milk production, a ration containing low to moderate amounts of digestible energy should be fed beginning 1 week before parturition and 1 week after parturition to aid in the prevention excessive milk production and, thus excessive milk intake by the foal. Specific preventative methods addressing *C. perfringens* include immunization mares with the use of a toxoid vaccine (Aluminum hydroxide adsorbed culture supernatant PLUS recombinant β2-toxoid. Vaccine strain is *Clostridium perfringens* Type A and carries genes for Alpha, β2 and CPE) that has recently been developed (2007) by Hagyard Equine Medical Institute (www.hagyardpharmacy.com). Other oral enteric protectants include the oral and/or administration of hyperimmunized plasma which was previously mentioned. Specific immune treatments for *C. perfringens* types C and D do provide some protection against alpha-toxin, but it is generally believed that this protection would be inadequate against *C. perfringens* type-A organisms.

**SALMONELLA**

*Salmonella* are gram negative, facultative, anaerobic bacteria, which usually can access to the intestinal tract via the fecal-oral route. *Salmonella* commonly infects foals between 12 hours and 4 months of age. Young animals are more susceptible to *Salmonella* infections maybe because of a less sophisticated or less well established microflora within the gastrointestinal tract. The most common source of exposure and infection in the foal is another horse. Often the mare herself in an asymptomatic carrier. Mares have been shown to shed *Salmonella* at or shortly after parturition despite having as many as 19 negative cultures before foaling. Observations of foalings revealed that all mares defecate during stage 2 labor and that contamination of fetal membranes and the perineum/udder of the mare was possible if *Salmonella* was in the feces. During udder seeking foals will have extensive contact with the perineum and therefore may be at risk of *Salmonella* ingestion.

Once *Salmonella* has overcome the host defense mechanisms (gastric acidity, intestinal flora, peristalsis, intestinal mucus and lactoferrin) the bacteria migrate through the enterocytes and access the lamina propria where they stimulate an inflammatory response. Both phagocytized and free *Salmonella* organisms travel via the lymphatics to regional lymph nodes where they persist in stimulating an inflammatory response. *Salmonella* can also reach circulation from efferent lymphatics. The neonate predisposition toward bacteremia and septicemia may be because of factors such as delayed gut closure at birth, immature cellular immune response and decreased complement activity. *Salmonella* enterotoxins, cytotoxins and generalized inflammation with in the bowel induces secretions of fluid from the intestinal epithelium.

**Clinical signs** of *Salmonellosis* are variable and can range from mild enteritis to severe septicemic shock. Diagnosis of *Salmonella* is demonstrated by a positive fecal or blood cultures. We have had foals present with fevers of unknown origin with no signs of diarrhea that have had positive blood and fecal cultures for *Salmonella*. Intermittent shedding of *Salmonella* is common
and therefore a minimum of three to five consecutive 1 gram fecal cultures taken 24 hours apart are recommended.

**Treatment** for salmonella is non-specific and is aimed at maintaining hydration and electrolyte balance. Antibiotic therapy even though it does not alter the clinical course of diarrhea or shedding of the organisms should be initiated in foals to help prevent bacteremia. Polymyxin B (6,000 IU/kg IV TID) diluted in 1 L of fluids, flunixin meglumine (0.25mg/kg TID IV) and pentoxifylline (7.5mg/kg PO BID) all have been shown to reduce the effects of endotoxinemia. Bismuth subsalicylate (1-3ml/kg PO Q4-8 Hrs) is also commonly used as a gastroprotectants secondary to its endotoxic and antiprostaglandin properties. J-5 plasma may also be given to aid in decreasing the systemic enterotoxin level.

**Prevention** of Salmonella consists of proper hygiene. Before the foal is able to nurse, the udder and perineal regions of the mare are to be thoroughly washed with dilute chlorohexidine or ivory soap and water. During an outbreak situation foals should also be intubated with 6-8 oz of colostrum prior to contact with the mare.

An experimental inactivated bacterin (Salmonella typhimurium and Newport) vaccine has been developed by Hagyard Equine Medical Institute and Dr. John Timmoney at the Gluck Research Center in Lexington KY. We have currently been using this vaccine on endemic farms since 2007.

**Enterococcus durans** (Group D Streptococcus)

*Enterococcus durans* is a gram positive coccus in the alimentary tract that has been implicated as a cause of enteritis in foals, piglets, calves and puppies. The author has documented *Enterococcus durans* as a cause of diarrhea in 5 of 7 foals that had developed diarrhea during the first 10 days of life. In one study conducted in Australia, *E durans* (isolated from a foal that had severe diarrhea) was experimentally infected in 7 foals (via stomach tube). All 7 foals developed profuse watery diarrhea within 24h of inoculation with varying degrees of depression, anorexia, abdominal tenderness and dehydration. The pathogenesis of diarrhea and enteric disease remains unknown. Diarrhea induced by *E. durans* is not associated with enterotoxin production or substantial mucosal injury. However decreased activity of brush border digestive enzymes such as lactase and alkaline phosphatase suggest that there is a direct mechanical interference with digestion and absorption at the brush border. The treatment for *E. durans* has not been adequately investigated but subjectively the β-lactams appear to help decrease the duration of the diarrhea (Ampicillin or Penicillin). The ideal treatment is to improve husbandry on the farm.

**Campylobacter jejuni**

*Campylobacter jejuni* is a rarely reported as a cause of diarrhea in foals. *Campylobacter spp.* are slender gram negative rods that damage the superficial mucosa. *Campylobacter jejuni* can be found in feces of healthy horses as well as healthy foals, so positive isolation from feces does not definitely indicate that the infection is the cause of diarrhea in that animal.

**NON INFECTIOUS**

**HYPOXIC ISCHEMIC ILEUS/NECROTIZING ENTEROCOLITIS**

Perinatal Asphyxia Syndrome produces hypoxic ischemic encephalopathy (HIE) resulting in neurological deficits ranging from hypotonia to grand mal seizures. Foal’s affected with perinatal asphyxia also experience gastrointestinal disturbances ranging from mild ileus and delayed gastric emptying to severe, bloody diarrhea and necrotizing enterocolitis (NEC). It has been postulated that when the preterm infant is stressed by periods of hypoxia or hypotension, blood flow is redistributed via input from adrenergic system away from the splanchnic bed. During the period of reperfusion, oxygen free radicals are generated; these free radicals can cause the tissue damage that is typically seen with reperfusion injury. If the hypoxic event is severe enough then necrotizing enterocolitis (NEC) can occur resulting in bloody diarrhea, penumatosis
intestinalis, ascites and/or intestinal perforation. A diagnosis of hypoxic ischemic ileus is presumptive when the patient has a history of peripartum asphyxia (placentitis, premature placental separation), negative fecal diagnostics for infectious diseases and abdominal ultrasonography reveals distended small intestine with decreased motility.

**Foal Heat Diarrhea**

Foal heat diarrhea is a lay man term for short periods of diarrhea seen in healthy foals aged 5 to 15 days of age that occurs during the the mare’s first estrus. Many attempts to identify the mare’s milk composition during the postpartum period/first estrus have not been useful to identify an association. Interesting, orphans and foals maintained on milk replacer often experience diarrhea during the same time period, therefore rule out the mare out as a cause. Results from one study supports the theory that the normal development of the foals gastrointestinal tract occurs during the first 2 weeks of life as the foal begins to consume solid feeds along with the inoculation of microflora (coprophagia) are responsible for the changes in the fecal composition during this period. Foals with the type diarrhea do not require therapy. If diarrhea persists for > 3 days duration along with clinical signs of lethargy then further diagnostics should be performed.

**Colic**

Abdominal pain in the foal can be a frustrating diagnostic challenge as the differential diagnosis are extensive (See Table 1). The approach to the neonate with a painful or distended abdomen includes history, type and dose of analgesics, administered and whether there are any animals affected with diarrhea. The age of the animal is also important in the determination of risks of certain conditions.

During the first 6 to 24 hours of age, congenital atresia of the colon, rectum, anus or meconium impactions are the most frequent causes of colic. In paint foals that are primarily white and whose dam and sire are overo are at risk for ileocolonic aganglionosis. Meconium is composed of glandular secretions from the gastrointestinal tract, amnionic fluid and cellular debris, which should be passed by 24-36 hours of age. In utero sepsis with associated hypoglycemia and sympathomimetic release can have bowel hypomotility and be at high risk for meconium impactions. Meconium impactions are more common in colts because of their narrow pelvic canal. The diagnosis of meconium impactions can be achieved by contrast radiographs, abdominal ultrasonography and/or proctoscopy. If routine warm water enemas do not relieve the impaction then hyperosmolar solutions (Hypertonic saline 3-4ml/kg per rectum) or acetylcysteine retention enemas may be used. The acetylcysteine enemas consists of mixing 200ml water, 8 grams of acetylcysteine powder, and 20 g of sodium bicarbonate. A well lubricated 12 or 14 Fr, cuffed Foley urinary catheter is introduced into the rectum and the cuff inflated. 200 ml of the retention enema solution is then slowly infused and the end of the catheter plugged. The catheter
is then taped to the foal’s tail and left in place for 15 minutes. These enemas can be repeated several times a day. If using the hypertonic solutions for more than 2 treatments in a 24-hour period the sodium status of the patient should be re-evaluated to prevent hypernatremia.

Additional therapy includes fluids and laxatives (120 ml of mineral oil SID to BID and/or milk of magnesia 30ml PO QID). Analgesics, such as flunixin meglumine 1.1mg/kg IV SID and butorphanol tartrate 1-2mg IV/IM Q 4-12 hours, may also be necessary to help control the foal’s discomfort.

Older foals 2-5 days of age are more likely to be suffering from intussusceptions, ruptured bladders, enteritis, gastroduodenal ulceration, inguinal hernias and small intestinal volvulus. Ultrasonography can be used to help diagnosis conditions that may be causing colic. Dynamically distended small intestine > 2.5cm in diameter with no motility and absence of gastric distention could be suggestive of a small intestinal volvulus. A large amount of peritoneal fluid with a history of infrequent urinations is suggestive of a ruptured bladder. Unfortunately severe abdominal pain is not pathognomonic for a surgical lesion. Tachycardia of excess of 150 beats per minute that is non-responsive to pain medication and in the absence of fever is suggestive of a surgical lesion.

**Lactase Deficiency (Dietary)**

Lactose intolerance has been diagnosed in foals as either:

1) Lactose malabsorption
   a. Physiological problem that arises from the consumption of too much lactose and the capacity for lactase to hydrolyze it (to glucose and galactose).
   b. An example is overfeeding or incorrectly prepared milk replacer

2) Secondary lactase deficiency⁴⁰
   a. A lactase deficiency that results to injury of the brush border (location of lactase enzyme) for example during enterocolitis.

3) Primary Lactase deficiency
   a. These animals have low or completely absent lactase concentrations
REFERENCES:
11) Darlington JW: Modified Nano-Bentonite Anti-Viral Activity Against the Herpes Simplex Virus Type 1, Rhinovirus Type 37, and Rotavirus. 19th International Conference of Antiviral Research. 2006. Poster.
TABLE 1

Differential Diagnoses of the Neonate with Gastrointestinal Failure

Meconium Retention
Enterocolitis
Uroperitoneum
Ileus
Herniation (Inguinal, Diaphragmatic or External)
Gastric Ulceration
Small intestinal volvulus
Intussusception
Necrotizing enterocolitis
Peritonitis
Intestinal Atresia
Ileocolonic aganglionosis
Large colon torsion
a Rotazyme, Abbott Laboratories, North Chicago, IL 60064; Wampole Laboratories, Cranberry NJ 08512
b LACTAID®, McNeil Consumer Healthcare, Fort Washington, PA 19034 USA
c Equine Rota Virus Vaccine, Fort Dodge Laboratories, Fort Dodge, IA 50501 USA
d Hagyard Anti-Diarrhea Gel, Hagyard Pharmacy, Lexington KY 40511 USA, www.hagyardpharmacy.com
e Lake Immunogenics Clostridium difficile Toxin a and B Antibody Select HI Plasma, Ontario NY 14519 USA
f Lake Immunogenics Clostridium perfringens Type A, C & D Antibody Select HI Plasma, Ontario NY 14519 USA