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**Neonatal Foal Diarrhea**

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**Take Home Message**

It is important to identify contagious causes of diarrhea to minimize the spread of disease on breeding farms. Diarrhea is one of the most common problems of newborn foals. Diarrhea can be a primary problem or secondary to sepsis. Searching for a specific pathogen in the feces of these foals is often unrewarding. Taking a thorough history is important to rule in/out age linked causes of diarrhea such as foal heat diarrhea, as well as to rule out other less common causes such as sand ingestion. Frequency of the diarrhea, suckling activity of the foal, and whether or not any other foals are affected on the premises are all very pertinent questions. Complications of diarrhea include severe dehydration, metabolic acidosis, electrolyte derangements, hypoproteinemia and bacteremia.

**Noninfectious Diarrhea in the Neonate**

1. **Foal heat diarrhea** is so named due to its occurrence during the first heat cycle post-partum (5-15 days). One study suggests that the cause of foal heat diarrhea is inoculation of microflora and maturational changes of the gastrointestinal tract. Foals typically do not demonstrate the signs of systemic illness observed with infectious causes. They are usually bright, alert and suckling with normal vigor.

2. **Nutritional** causes of diarrhea in neonates are minimal. The most common occurrence includes excessive milk intake that may occur when feeding orphaned foals. Excessive intake of milk will overload the ability of the small intestine to digest and absorb and results in milk entering the colon where it is fermented producing osmotically active sugars and acids. Transient lactase deficiency has been proposed in foals. It has been postulated that foals develop lactase deficiency secondary to infection of rotavirus or *Clostridium difficile*. Lactase is produced in the mucosal cells and these cells are damaged by rotavirus. Foals with suspected lactase deficiency can be treated with lactase enzyme (6000-9000 Food Chemical Codex units/ 50 kg PO q 3-8 hours).

3. **Asphyxia related gut injury** occurs if a foal suffers a lack of oxygen at birth from complications such as dystocia or umbilical cord problems. The foal can become intolerant to feeding, display signs of colic and develop abdominal distention. The foal can develop gastrointestinal reflux and diarrhea. Abdominal ultrasound would reveal ileus and possible thickening of the gastrointestinal tract. Treatment includes supportive care, parenteral nutrition and antimicrobials to prevent sepsis.
4. **Miscellaneous causes** of noninfectious diarrhea include gastric ulceration, ingestion of sand and irritants such as the mare’s tail hairs or ropes. Gastric ulceration will be discussed by Dr. Sanchez in another lecture. Digital examination of the rectum may reveal sandy material in foals that have consumed excessive quantities of sand. Abdominal radiographs can confirm the presence of sand. Treatment for sand includes small amounts of mineral oil and psyllium via nasogastric tube.

**Infectious Diarrhea in the Neonate**

Causes of diarrhea may be divided into bacterial, viral and parasitic. Isolation of an organism from the feces of foals with diarrhea does not directly indicate that the diarrhea is caused by that agent as it could be normal flora. Recovery of *Clostridium perfringens* (biotype A), *Rhodococcus equi*, *Bacteroides fragilis*, or rotaviruses are examples of potential enteric pathogens that may be recovered from the feces in the absence of disease. Unfortunately, our knowledge of normal flora is lacking. Does the fact that *Aeromonas hydrophila* is more frequently recovered from feces of foals with diarrhea than from healthy animals indicate that this bacterium is responsible for the diarrhea, or does it merely reflect a change in normal flora and bacterial shedding in response to changes induced by a different pathogen? As with calves, the isolation of two or more potential intestinal pathogens from foals with diarrhea is not uncommon.

**Aerobic Bacterial Pathogens**

1. **Salmonellosis**: Spectacular outbreaks of Salmonellosis are possible in horses of any age, but most occurrences in foals occur as isolated cases. The mare appears to be the primary source of infection and usually both the dam and foal are fecal positive for the pathogen. It is rare for both to demonstrate signs of disease. Most affected foals have moderate to severe clinical signs that include fever, diarrhea, dehydration, profound depression and reduced appetite. Diarrhea can vary in both consistency and volume, and may contain blood. Colic is common in the early stages of the disease. A complete blood count usually reveals neutropenia, with a left shift and toxicity, but is replaced by a rebound neutrophilia as the disease becomes chronic. The fibrinogen is usually elevated. Extra-intestinal disease is common in foals less than 2 months of age as consequence to bacteremia. These include bacterial uveitis, infectious synovitis, osteomyelitis, pneumonia, and meningitis.

**Diagnosis**

a. **Blood culture**: This is particularly useful in foals less than 1 month of age, as young foals with intestinal Salmonellosis are frequently bacteremic.

b. **Fecal culture**: Transport using suitable transport media (e.g., Ames aerobic culture media). Samples can be transported in selenite broth if processed within 24 hours of collection. Five samples must be submitted before the foal can be declared negative.

c. **Fecal PCR**: This technique appears to be highly sensitive and a positive result may carry greater importance in a foal than adult horse with diarrhea.

**Treatment**: In contrast to adults, most foals with *Salmonella* infection require aggressive and early antibiotic treatment. Appropriate first line choices include 3rd generation cephalosporins or aminoglycosides but should be guided by sensitivity patterns. Unfortunately, secondary sites of infection, particularly osteomyelitis, may develop and persist in the presence of antibiotic therapy. These complications may not be detected clinically for weeks after the
onset of enteric disease. Bismuth subsalicylate is commonly used in foals with diarrhea. Its anti-diarrheal action is through stimulation of fluid and electrolyte absorption and by inhibiting the synthesis of prostaglandins (when hydrolyzed to salicylic acid) involved in intestinal inflammation. Bismuth subsalicylate also binds bacterial toxins and is thought to have a bactericidal action. The use of motility-modifying agents, such as atropine or loperamide, is contraindicated in foals with enteric infections where bacteria or bacterial toxins may invade or damage the intestinal mucosa (e.g., clostridial infections, *Salmonella*). Loperamide may be useful in other forms of diarrhea, but prolonged use is not recommended. If clinical improvement is not apparent by 48 – 72 hours then further use is unlikely to be helpful.

2. *Escherichia coli* is the most common cause of systemic sepsis in newborn foals, but is an uncommon primary enteric pathogen. There are reports that suggest that *E. coli* can mediate diarrhea in foals less than one month of age. The diarrhea is profuse, watery, but non-fetid.\(^4\) *E. coli* is a common microbe cultured from manure of normal horses. To determine if it is the cause of infection PCR for the toxin gene should be performed.

3. *Enterococcus* (Group D *Streptococcus* *durans*) is an organism that has been implicated as a cause of diarrhea in several species including foals, pigs, calves, and pups.\(^5\) *Enterococcus durans* is commonly isolated from the feces of young foals with diarrhea, although often with other potential pathogens. Tzipori and others concluded that the organism colonized the small intestinal mucosa and was associated with mild-to-moderate pathology.\(^5\) It is therefore likely that the severity of diarrhea would be inversely related to age.

4. *Rhodococcus equi* infection of the respiratory tract is frequently associated with changes within the Peyer’s patches and mesenteric lymph nodes, but diarrhea is rare. There is a syndrome of ulcerative enterocolitis attributed to *R. equi*, but establishing an ante-mortem diagnosis is difficult as fecal culture of the organism is common.

Other aerobic bacteria implicated in infectious diarrheas include *Aeromonas hydrophila*, *Yersinia enterocolitica*, and *Campylobacter* species but these are rare.

**Anaerobic Bacterial Pathogens**

1. Intestinal Clostridiosis can be caused by *Clostridium perfringens* biotypes types A and C and *Clostridium difficile*. These gram positive organisms can be found in the intestinal tracts of domestic animals and are widely distributed throughout the environment, including the soil. They produce potent exotoxins which are responsible for a variety of intestinal diseases in domestic animals. Enteric disease induced by *Clostridium* species are recognized more commonly during the early neonatal period. There are reports of *C. perfringens* biotypes A, B, C, D and E being associated with enteric disease of foals, but most studies suggest that biotypes A and then C are the most important.\(^6\)

Classically the disease induced by *C. perfringens* biotype C is associated with hemorrhagic diarrhea, abdominal distention, colic, circulatory shock and a high mortality (83%).\(^7\) The
disease often occurs within the first 48 hours of life and is most commonly seen in vigorous foals with adequate passive transfer.

In recent years, there has been an emergence of enteric disease in newborn foals associated with *C. perfringens* biotype A. Clinical signs are more variable, but may include transient bloody stool, colic and fever. Mortality is reduced (28%) when compared with disease induced by *C. perfringens* biotype C. The role of this biotype is frequently confounded as it appears to be commonly present in the feces of healthy young foals. 

Likewise, the role of *C. difficile* in foal diarrhea is not clear. A well-defined cause of neonatal enterocolitis in foals less than 4 days of age, this organism has received a lot of attention in recent years as a potential enteric pathogen of adult horses. Prevalence varies with geographic location, but *C. difficile* appears to be a rare isolate in older suckling foals.

**Diagnosis**

- **Fecal culture:** Samples should be collected and shipped in an appropriate container (Port-a-Cul anaerobic tubes, Becton Dickinson). The isolation of *C. difficile* is usually considered significant in foals of all ages, but it is not uncommon to identify foals that are culture positive but toxin negative. Recovery of *C. perfringens* from diarrheic foals is also of questionable significance as the organism is commonly present in the feces of healthy foals, particularly *C. perfringens* biotype A.

- **Identification:** The genes that encode the Clostridial toxins can be amplified and categorized using PCR techniques. All *C. perfringens* isolates contain an alpha toxin. Further separation into biotypes A through E is based on identification of additional toxins produced by the bacteria. The exception is a *C. perfringens* isolate that is yet to be biotyped, but contains the alpha toxin and a β₂ toxin. The latter toxin has similar biological activity to the β toxin, but has no significant amino acid homology with that toxin. This organism has been isolated from both adult horses and foals with diarrhea.

- **Toxin assays:** Samples should be shipped directly to a diagnostic laboratory immediately or transported on ice and shipped overnight. The traditional method for toxin identification within intestinal contents or fecal samples is through mouse inoculation. Commercial assays for toxins A or B of *C. difficile* are reliable if the samples are handled appropriately. If samples are exposed to room air > 15 minutes the toxin degrades. An additional commercial assay is available for *C. perfringens* enterotoxin (CPE), but concerns exist as to sensitivity, specificity and the positive predictive value of this test in clinical cases.

- **Gram stain of feces:** Large number of Gram positive rod-shaped bacteria are seen on fecal Gram stain. Spore stains can be requested, but rarely provide useful additional data.

- **Blood culture:** Highly recommended in young foals as many foals are bacteremic with *C. perfringens* (usually biotype A) and rarely *C. difficile*.

**Treatment**

Treatment should consist of antimicrobial agents including potassium or sodium penicillin and metronidazole. Additional support includes fluid therapy, correction of electrolyte
derangements, plasma or hetastarch for low oncotic pressure, sodium bicarbonate to correct metabolic acidosis and the use of inotropes and vasopressors to maintain blood pressure. Di-tri-octahedral smectite (Biosponge, Platinum Performance) neutralizes *C difficile* toxins A and B and *C perfringens* enterotoxins in vitro. Saccharomyces boulardii has been shown to help decrease the severity and duration of clinical signs in adult horses. The use of Lactobacillus pentousus did not prevent diarrhea in foals and is not recommend. C. perfringens biotype C anti-toxin has been administered orally but scientific data has not confirmed the effectiveness of this treatment. Anecdotal success has been reported with the use of commercial type C & D toxoid in pregnant mares. There is no documentation of safety or efficacy of this vaccine.

2. *Bacteroides fragilis* is an intestinal pathogen of foals. Unfortunately isolation of the organism from diarrhea samples does not confirm diagnosis, as the bacterium occurs in both enterotoxigenic and non-toxigenic forms. Enterotoxigenic strains of *B. fragilis* are associated with diarrhea in several species including lambs, calves, pigs, humans and foals. These pathogenic strains are non-invasive, but produce a 20 kD heat-labile toxin which induces mucosal inflammation. Limited data from foals indicate that *B. fragilis* commonly is isolated with other pathogens. Diagnosis is achieved by culture of the organism and then verification of toxin producing strains by arbitrarily-primed PCR or more traditionally, through isolated intestinal loop inoculation. Treatment involves administration of metronidazole and supportive therapy.

**Viral Intestinal Disease**

1. **Rotavirus**: Group A rotavirus is the most common cause of infectious diarrhea in foals. Typically, several foals are affected over a short period of time. The disease is highly contagious and has a very short incubation period. The severity of disease is determined by immune status, inoculation dose, and age. The basis of the diarrhea is not fully known, but likely involves brush border enzyme deficiency (lactase), leading to inadequate digestion and osmotic diarrhea in the colon. The virus invades the villus tip epithelium resulting in loss of absorptive cells. A non-structural glycoprotein, NSP4, is a potential viral cytotoxin and enterotoxin.

   The diagnosis of rotavirus is often made on the basis of epidemiological findings, physical examination findings (diarrhea, depression, reduced appetite, ± fever), and submission of samples from representative animals. Fecal antigen tests (e.g., Virogen Rotatest and Rotazyme) are sensitive and provide rapid confirmation. Submission of fecal samples for electron microscopy (EM) is an effective means of establishing a diagnosis. Treatment is supportive using a combination of intravenous and oral replacement fluids. A maternal vaccine is available and may confer modest protection.

2. **Coronavirus**: There are recent reports of coronavirus acting as a primary pathogen in young immunocompetent foals. Previously foals with immune dysfunction, such as SCID Arabian foals, were considered to be at greatest risk. It is unlikely that coronavirus infection is responsible for outbreaks of foal diarrhea. Diagnosis is possible with fecal ELISA or EM.
Protozoan Intestinal Diseases

1. Cryptosporidium: The role of cryptosporidium in foal diarrhea remains controversial. Infection rates have been reported between 15 and 31% in suckling foals. Cryptosporidium has been associated with fatal outcomes in foals and should be considered as a cause of diarrhea in compromised, hospitalized neonates. There are several methods commonly used to detect oocysts in fecal samples including acid-fast staining, immunofluorescence assay, and flow cytometry. Submission of fecal samples to a laboratory should specifically state that detection of cryptosporidium is required, as expertise is usually necessary to detect the small oocysts. Treatment is generally supportive, and centers on fluid and electrolyte replacement. Specific drug therapy could be attempted, such as paromomycin, but there are no efficacy data in foals. Prevention includes environmental disinfection and isolation of infected foals.

2. Giardia: Giardia infection rates in foals have been reported to be as high as 35%, but data to associate shedding with disease is lacking. There have been isolated cases of suckling foals with diarrhea and high Giardia counts that have responded to a short course of metronidazole.

Parasitic Intestinal Disease

Strongyloides westeri may cause diarrhea in neonates if a large amount of larvae are acquired from the mare’s milk after birth. Most farms will routinely deworm their mares shortly after foaling to reduce the incidence of this disease.

Conclusion

It is important to identify a laboratory that is capable of providing an in-depth fecal analysis. Most commonly this is a state diagnostic laboratory. It is also critical to consider likely differentials when requesting tests and understand the relevance of a positive test result. Treatments continue to be primarily supportive, but often include metronidazole or specific antibiotic therapy if Salmonella is identified.

References


