Infectious Diarrhea in Foals

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1. Introduction

The range of infectious agents that cause diarrhea in foals is poorly described, at least when compared to other domesticated species. Recently, several new agents have been incriminated as causes of diarrhea in newborn and suckling foals. In addition, there are new diagnostic tests available that may aid in differentiating new and established causes of diarrhea. Many of these tests involve primary bacterial culture with subsequent molecular analysis.

The approach to diagnosis requires knowledge of likely pathogens, what tests are available, and how to interpret data from the lab. In addition, the type of samples to be requested should be guided by the animal’s age, the number of foals affected, and physical examination findings.

Isolation of an organism from the feces of foals with diarrhea does not directly indicate that the diarrhea is caused by that agent. *Clostridium perfringens* (biotype A), *Rhodococcus equi*, *Bacteroides fragilis*, and rotavirus are examples of potential enteric pathogens that may be recovered from feces in the absence of disease. Unfortunately, our knowledge of normal flora or changes that occur in the flora in response to disease is lacking. For example, does the fact that *Aeromonas hydrophila* is more frequently recovered from the feces of foals with diarrhea than from those of 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? Controlled inoculation studies are required to verify a more definitive role for some of these potential pathogens. In addition, the recovery of two or more potential intestinal pathogens from foals with diarrhea is not uncommon.

2. Specific Agents Associated with Infectious Foal Diarrhea

Anaerobic Bacterial Pathogens

*Intestinal Clostridiosis*

The common causative agents of this condition are *Clostridium perfringens* biotypes 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 that 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 and there are reports of biotypes A, B, C, D, and E being associated with enteric disease of foals; most studies suggest that biotypes A and then C are the most important.
Classically, disease induced by *C. perfringens* biotype C is associated with hemorrhagic diarrhea, abdominal distention, colic, circulatory shock, and high mortality. Disease often occurs within the first 48 hours of life and is most commonly seen in vigorous foals with high milk intake. The diagnosis is confirmed by identifying the toxin within the feces or intestinal lumen (by mouse inoculation). Recovery of the organism and biotyping by toxin gene identification (PCR) may increase the accuracy of diagnosis short of toxin identification. Treatment is often unrewarding but should consist of antimicrobial agents (including potassium or sodium penicillin and metronidazole), nonsteroidal anti-inflammatory agents, plasma, and *C. perfringens* biotype C antitoxin. Total parenteral nutrition should be considered if aggressive treatment is pursued. Probiotics may be beneficial as part of a treatment protocol or as preventative therapy in other newborn foals on the property. Anecdotally, success has been reported with the use of commercial type C & D toxoid in pregnant mares.

In recent years, an emergence of enteric disease associated with *C. perfringens* biotype A has been seen in newborn foals. Clinical signs are variable but may include transient bloody stool, colic, and fever. Mortality is reduced when compared with disease induced by *C. perfringens* biotype C. The role of this biotype is frequently confounded because it appears to be commonly present in the feces of healthy young foals.²

Likewise, the role of *C. difficile* in juvenile diarrhea is not clear. A well-defined cause of neonatal enterocolitis in foals less than 4 days old, 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. Treatment is as for *C. perfringens* biotype C minus the commercial type C & D antitoxin.

**Fecal culture.** Samples should be collected and shipped in an appropriate container (Port-a-Cul aerobic tubes).³ 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.³ Recovery of *C. perfringens* from diarrheic foals is also of questionable significance because the organism, particularly *C. perfringens* biotype A, is commonly present in the feces of healthy foals.

**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 the identification of additional toxins produced by the bacteria. The exception is a *C. perfringens* isolate that is yet to be biotyped but that contains the alpha toxin and a β2 toxin. The latter toxin has biological activity similar to the β toxin but has no significant amino acid homology with that toxin. This organism has been isolated both from adult horses and foals with diarrhea.

**Toxin assays.** Samples should be delivered 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 by mouse inoculation. Commercial assays for *C. difficile* toxins A or B are reliable if the samples are handled appropriately. 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 numbers 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 because many foals are bacteremic with *C. perfringens* (usually biotype A) and, rarely, *C. difficile.*

**Bacteroides fragilis**

It is likely that *Bacteroides fragilis*, a gram-negative anaerobic rod, is an intestinal pathogen of foals. Unfortunately, isolation of the organism from diarrhea samples does not confirm diagnosis because the bacterium occurs both in enterotoxigenic and non-toxigenic forms. Enterotoxigenic strains of *B. fragilis* are associated with diarrhea in several species, including lambs, calves, pigs, humans, and foals.⁴ These pathogenic strains are noninvasive but produce a ~20 kD heat-labile toxin that induces mucosal inflammation. Limited data from foals indicate that *B. fragilis* is commonly isolated with other pathogens.

Diagnosis is achieved by culturing the organism and then verifying toxin-producing strains with arbitrarily primed PCR or, more traditionally, with isolated intestinal loop inoculation.⁵ Treatment involves administration of metronidazole and supportive therapy.

**Aerobic Bacterial Pathogens**

**Salmonellosis**

Spectacular outbreaks of salmonellosis are possible in horses of any age⁶ but most occurrences in foals occur as isolated cases. The mare appears to be the primary source of infection and both the dam and the foal usually 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 both in 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, which is replaced by a rebound neutrophilia as the
disease becomes chronic. The fibrinogen usually is elevated.

Extraintestinal disease as a consequence of bacteremia is common in foals less than 2 months old. These extraintestinal diseases include bacterial uveitis, infectious synovitis, osteomyelitis, pneumonia, and meningitis.

Blood culture. This is particularly useful in foals less than 1 month old because young foals with intestinal salmonellosis frequently are bacteremic.

Fecal culture. Transport using suitable media (e.g., Ames aerobic culture media). Samples can be transported in selenite broth if processed within 24 hours after collection.

Fecal PCR. This technique appears to be highly sensitive and a positive result may carry greater importance in a foal than in an 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 third-generation cephalosporins or aminoglycosides, which 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 antidiarrheal action is achieved by stimulation of fluid and electrolyte absorption and by inhibiting the synthesis of the 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 or 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, further use is unlikely to be helpful.

Escherichia coli

Escherichia coli is the most common cause of systemic sepsis in newborn foals but it is an uncommon primary enteric pathogen. There are reports that suggest that E. coli can mediate diarrhea in foals less than one month old. The diarrhea is profuse and watery but nonfetid. Enteropathogenic strains of E. coli (0111a, K792) caused classical ultrastructural changes to the intestinal microvilli of ileal explants harvested from month-old foals. Recovery of E. coli from feces is very common but these isolates typically lack the appropriate virulence factors required to create intestinal disease.

Diagnosis is achieved by culture from feces and then detecting virulence factors with PCR. A heavy growth of mucoid E. coli on agar plates would increase the level of suspicion.

Enterococcus (Group D Streptococcus) durans

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

Rhodococcus equi

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 because fecal culture of the organism is common.

Other Aerobic Bacteria Implicated in Infectious Diarrhea

These bacteria include Aeromonas hydrophila, Yersinia enterocolitica, and Campylobacter species. Much of the data incriminating Aeromonas hydrophila as a potential pathogen of foals stems from work done in the UK in the early 1990s.

Viral Intestinal Disease

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. Severity of disease is determined by immune status, inoculation dose, and, most importantly, age. The basis of the diarrhea is not fully known but it likely involves brush border enzyme deficiency, which leads to inadequate digestion of substrate and osmotic diarrhea in the colon. Recent attention has been given to the membrane-spanning nonstructural glycoprotein NSP4 as a potential viral cytotoxin and enterotoxin. The enterotoxin is released from rotavirus-infected enterocytes and is a specific noncompetitive inhibitor of the Na(+)•D-glucose symporter. The protein also enhances chloride secretion through a signal transduction pathway.

The diagnosis of rotavirus is often made on the basis of epidemiological findings (large number of cases), physical examination findings (diarrhea, depression, or reduced appetite, with or without fever), and samples from representative animals. Fecal antigen tests (e.g., Virotek Rotatest and Rotazyme) are sensitive and provide rapid confirmation. Submitting fecal samples for electron microscopy (EM)
is also an effective means of establishing a diagnosis.

Treatment of rotaviral diarrhea is supportive and uses a combination of intravenous and oral replacement fluids. Antibiotics are not indicated unless the foal is less than 2 weeks old. A maternal vaccine is available and may confer modest protection.

Coronavirus

There are recent reports of coronavirus acting as a primary pathogen in young immunocompetent foals.\(^1\) Previously, foals with immune dysfunction, such as severe combined immunodeficiency disease (SCID) Arabian foals, were considered to be at greatest risk. It is unlikely that coronavirus infection is responsible for outbreaks of foal diarrhea. There have also been reports, published and unpublished, of parvovirus and breda virus causing diarrhea in foals.

Protozoan Intestinal Diseases

Cryptosporidium

The role of cryptosporidium in foal diarrhea remains controversial. Infection rates have been reported between 15% and 31% in suckling foals.\(^13\) Cryptosporidium has been associated with fatal outcomes in foals.\(^14\) Foals at greatest risk for cryptosporidium-induced diarrhea are those with primary immunodeficiencies. There are several methods commonly used to detect oocysts in fecal samples, including acid-fast staining, immunofluorescence assays, and flow cytometry. Acid-fast staining is very sensitive but is less specific than the other techniques.\(^15\) Submission of fecal samples to a laboratory should specifically state that detection of cryptosporidium is required because expertise usually is necessary to detect the small oocysts.

Treatment is generally supportive and centers on fluid and electrolyte replacement. Specific drug therapy such as paromomycin could be attempted but there are no efficacy data available for foals. Prevention includes environmental disinfection and isolation of infected foals.

Giardia

Giardia infection rates in foals have been reported to be as high as 35% but data associating shedding with disease are lacking. There have been isolated cases of suckling foals with diarrhea and high Giardia counts who have responded to a short course of metronidazole.

3. Conclusion

It is important to locate a laboratory that is capable of providing in-depth fecal analysis. Most commonly, this is a state-run diagnostic laboratory. It is also critical to consider likely differentials when requesting tests and to 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 and Footnotes


\(^a\)Becton Dickinson, Franklin Lakes, NJ 07417.
\(^b\)Boehringer Ingelheim, Germany.
\(^c\)Virogen Rotatest, Wampole Laboratories, Cranbury, NJ 08512; Rotazyme, Abbott Laboratories, Abbott Park, IL 60064.