Diarrhoea in foals

Diarrhoea is one of the most common clinical complaints in foals and can be associated with significant morbidity and mortality. Clinical presentation can vary from mild, transient diarrhoea through to severe enterocolitis with significant systemic complications. There are numerous infectious and non-infectious aetiologies, the prevalence of which varies between age groups. Supportive care for foals with diarrhoea includes fluid therapy, antimicrobials, ulcer protection and analgesia. It is important that treatment is initiated promptly and re-evaluated frequently in response to clinical progression, particularly in neonates that are susceptible to rapid deterioration. Many causes of diarrhoea in foals are contagious and strict biosecurity protocols should be implemented to try and control the spread of disease.

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Diarrhoea is one of the most common clinical complaints in foals and is associated with significant morbidity and mortality (Cohen, 1994). Clinical presentation ranges from mild, transient alteration in faecal consistency with minimal systemic illness, through to severe enterocolitis with marked metabolic complications, such as acidosis, hypovolaemic shock, hypotension and bacteraemia. Enterocolitis in foals is usually evident, with the presence of a wet tail or diarrhoea down their hindlimbs. Other signs include dullness, reduced interest in nursing, abdominal distension or colic. Foals with chronic diarrhoea may have evidence of hair loss over their hindquarters. Less common signs include rectal prolapse or swelling of the vulva.

Pathophysiological mechanisms that can play a role in inducing diarrhoea in foals include complications secondary to fluid and electrolyte losses, destruction of the villous tips (resulting in the loss of important enzymes such as lactase) and inflammation of the intestinal tract. Intestinal tract inflammation can lead to epithelial barrier damage, which allows normal intestinal bacteria to translocate across the intestinal wall, increasing the risk of generalised septicaemia and/or localised sepsis. One study reported that over 50% of foals with diarrhoea were bacteraemic, based on blood cultures at the time of admission (Hollis et al, 2008).

There are numerous infectious and non-infectious aetiologies, the prevalence of which varies between age groups (Magdesian, 2005). *Table 1* summarises some of the potential causes of diarrhoea in different age groups.

Non-infectious causes of diarrhoea

Foal heat diarrhoea is a self-limiting condition that occurs in 75-80% of foals, aged between 5 and 15 days. Diarrhoea is usually transient, lasting 3–4 days, and foals typically remain bright and systemically well (Masri et al, 1986). Attempts have been made to identify a causative agent in the mare's milk around the time of oestrus, but these have been unsuccessful (Johnston et al. 1970). Orphan foals on milk replacer have also been shown to develop diarrhoea, at similar ages (Magdesian, 2005). Therefore, the association with foal heat appears to be temporal. It is more likely that foal heat diarrhoea is associated with alterations in the foal's microbiota during this early developmental period. However, the exact cause remains unclear (Kuhl et al, 2011). No treatment is required and diarrhoea generally subsides within several days, but it is important these foals are monitored closely as foal heat diarrhoea can resemble early enteritis and rapid clinical deterioration is possible.

A common cause of diarrhoea in hospitalised neonatal foals is perinatal asphyxia syndrome (PAS), associated with gastrointestinal dysfunction. These foals typically have associated risk factors, such as dystocia, caesarean section or inadequate oxygen following delivery, and usually present with signs of PAS in other body systems (most commonly neurological dysfunction). It is hypothesised that hypoxic injury of the gastrointestinal tract may lead to ischaemic damage to the enterocytes. In addition to diarrhoea, foals with PAS associated gastrointestinal dysfunction may display other signs, including gastrointestinal reflux, intolerance of enteral feeding or abdominal distension (Magdesian, 2005). Because multiple body systems tend to be involved, intensive care is generally required. A more serious and often fatal condition reported in hospitalised foals is necrotising enterocolitis (NEC). This is the most frequent and lethal disorder affecting preterm human infants and is associated with disruption of the intestinal barrier leading to intestinal necrosis, multiorgan failure and death (Good et al, 2014). The pathophysiology appears to be multifactorial and involves a complex interaction of immaturity, gastrointestinal mucosal injury, enteral milk feeding and bacterial invasion (Noerr, 2003). There has also been some recent evidence suggesting that NetF-positive type A Clostridial perfringens may play an important role in the development of NEC in foals (Mehdizadeh et al, 2015).

Foals with NEC require intensive care with intravenous fluid therapy and broad spectrum antimicrobials. Enteral feeding should be avoided on account of its potential role in the disease, so paren-

teral nutrition is often required. Even with intensive care, the prognosis for survival in these cases is poor.

Another non-infectious cause of diarrhoea in foals is dietary intolerance. This is most commonly noted in foals receiving milk replacers, particularly if the replacer is not made up correctly (too diluted or too concentrated). The ingestion of abnormal material, for example sand, can also result in diarrhoea because of the mechanical irritation to the gastrointestinal tract.

Diarrhoea can be associated with primary gastric ulceration in foals. Other frequently reported signs include bruxism, ptyalism, dorsal recumbency, colic, ill thrift, poor hair coat and lethargy. It is also important to note that foals with enteritis are at increased risk of developing ulcers. This occurs secondarily to physiological stress, which can include haemodynamic derangements, anorexia, inflammatory mediators and endocrine disturbances (Furr et al, 1992).

Infectious causes

Viral infection

Rotavirus is the most commonly detected infectious agent in foals. In one study, it was reported to be responsible for between 35–90% of cases up to 3 months of age (Slovis et al, 2014). Clinical disease ranges from mild self-limiting diarrhoea, through to profuse watery diarrhoea and significant dehydration, in which case electrolyte abnormalities can occur. Rotavirus infection is most commonly seen in foals between 5 and 35 days, the majority being at the younger end of this range. Although older foals can be infected, clinical disease tends to be more mild in this age group.

The virus infects the epithelial tips of the villi of the small intestine, resulting in cell lysis and blunting of the villous tips. This leads to a loss of the absorptive capacity of the villi. Villous injury also results in decreased production of disaccharidases, particularly lactase, which results in impaired digestion of lactose, further contributing to the development of diarrhoea.

Rotaviruses are highly contagious and morbidity can be up to 100% in outbreak situations. Faecal-oral transmission can occur directly or indirectly (via fomites), and the virus can persist in the environment for several months. The incubation period is 1–4 days (Bailey et al, 2013) and the virus is shed in high concentrations in the faeces of infected animals. Strict isolation protocols are therefore essential to help control the spread of disease. Treatment involves supportive care and although morbidity is high, the prognosis for survival is generally good. Vaccination of mares during gestation is commonly performed to help prevent rotavirus outbreaks (Powell et al, 1997).

Equine Coronavirus (ECoV) has been identified in the faeces of foals with diarrhoea. However, its pathogenicity and role in enteric disease are not fully understood. It has been reported that healthy foals (without gastrointestinal disease) were infected with ECoV equally as often as unhealthy foals (with gastrointestinal disease), suggesting a low pathogenicity of ECoV in foals (Slovis, 2014). Equine adenovirus has also been identified in the faeces of foals with diarrhoea, but the role of this virus in neonatal diarrhoea remains unclear (Corrier et al, 1982).

Bacterial infection

Clostridium difficile and *Clostridium perfringens* are the primary bacterial agents of concern in foals. Although both organisms can

Table 1. Infectious and non-infectious causes of diarrhoea in foals

Age group	Infectious causes	Non-infectious causes
0-14 days	**Viral infection** • Rotavirus • Coronavirus/adenovirus (usually seen in immunocompromised foals) **Bacterial infection** • *Clostridium difficile* • *Clostridium perfringens* • *Escherichia coli* • Salmonella **Fungal infection** • *Candida*/*Mucor* spp. (usually seen in immunocompromised foals) **Protozoal infection** • *Cryptosporidium* spp.	• Foal heat diarrhoea • Nutritional causes (such as errors in feeding or lactose intolerance) • Perinatal asphyxia syndrome • Necrotising enterocolitis
2 weeks – 2 months	**Viral infection** • Rotavirus • Equine Coronavirus/ adenovirus (usually seen in immunocompromised foals) **Bacterial infection** • *Clostridium difficile* • *Clostridium perfringens* • *Escherichia coli* • *Salmonella* **Fungalinfection** • *Candida*/*Mucor* spp. (immunocompromised foals) **Protozoal infection** • *Cryptosporidium* spp. **Parasitic infection** • *Strongyloides westeri*	• Nutritional causes (such as errors in feeding or lactose intolerance) • Luminal irritants (such as sand enteritis • Gastric ulceration
Over 2 months	**Viral infection** • Rotavirus • Coronavirus **Bacterial infection** • *Clostridium difficile* • *Clostridium perfringens* • *Escherichia coli* • *Salmonella* • *Lawsonia intracellularis* • *Rhodococcus equi* **Fungal infection** • *Candida*/*Mucor* spp (immunocompromised foals) **Parasitic infection** • *Strongyloides westeri* • *Parascaris equorum* • *Strongylus vulgaris*	• Nutritional causes (such as errors in feeding or lactose intolerance) • Luminal irritants (such as sand enteritis • Gastric ulceration

be found in healthy foals, they are more frequently identified in foals with enterocolitis (Frederick et al, 2009; Weese et al, 2001). The development of disease is associated with toxin producing strains of the bacteria. Risk factors for the development of disease include previous use of antimicrobials and stressors such as hospitalisation, travel and weaning. Cases can occur either sporadically or in outbreak situations.

The different types of *Clostridium perfringens* are determined based on their pattern of toxin production. The best understood pathogens in foals are types A and C (East et al, 1998). Beta-toxin is a major virulence factor of *Clostridium perfringens* and appears to be the primary toxin responsible for intestinal injury (Uzal et al, 2012). In contrast, alpha-toxin is not thought to be a significant enteric virulence factor (Jones, 2000). Enterotoxin is reported to be produced by 2–6% of all isolates, but its role as a virulence factor remains to be proven.

Clostridium perfringens can result in severe enterocolitis in foals, with rapid progression and high mortality rates reported (Traub-Dargatz and Jones, 1993; East et al, 1998). Presenting clinical signs include colic, haemorrhagic diarrhoea with significant systemic inflammation and shock, and sudden death. This clinical syndrome appears to be most prominent in neonatal foals (East et al, 1998). A less severe form of disease (mild, transient diarrhoea) has also been reported and tends to be recognised in older foals (Jones, 2000). In one study, it was reported that foals infected with *Clostridum perfrigens* type C had significantly higher mortality than those infected with type A (East et al, 1998). *Clostridium difficile* can also be a cause of enteritis in foals, often requiring antimicrobial administration or hospitalisation. In contrast to adults, foals can be asymptomatic carriers. The organism has been found in almost one third of healthy foals less than 14 days old (Baverud, 2002). Pathogenic strains of *Clostridium difficile* produce toxins that are major virulence factors, with toxins A and B being the best described in foals. Although antimicrobial therapy is a risk factor for disease, spontaneous cases of *Clostridium difficile* associated diarrhoea can also occur without previous antimicrobial therapy (Jones et al, 1987).

Severe haemorrhagic enterocolitis, with signs of abdominal distension, colic, systemic inflammation and rapid deterioration, has been reported in neonatal foals with *Clostridium difficile* (Jones et al, 1988). However, clinical disease in older foals can vary from mild to severe diarrhoea (Jones et al, 1987). *Salmonella* spp. are well recognised pathogens associated with diarrhoea and septicaemia in foals. The prevalence of *Salmonella* spp. has not been extensively investigated in foals, but when identified their presence is considered significant. Clinical signs include moderate to severe diarrhoea, pyrexia, depression and inappetence. Foals with salmonellosis should be monitored closely for evidence of sepsis and for signs of localised infections such as uveitis, synovitis and osteomyelitis (Magdesian, 2005). All neonatal foals with enteric salmonellosis should be treated with systemic antimicrobials that are effective against salmonellae (such as aminoglycosides or third-generation cephalosporins). Although primarily a respiratory pathogen, *Rhodococcus equi* can cause extra-pulmonary disease including enterocolitis, abdominal abscessation, peritonitis and hepatitis (Reuss et al, 2009). Although the number of foals presenting with diarrhoea is likely small, it should be considered as a potential cause in foals over 30 days of age, particularly in those with respiratory diseases or from farms with a history of *Rhodococcus equi* infection. *Lawsonia intracellularis* is an intracellular bacteria that infects young horses, causing an intestinal disease known as equine proliferative enteropathy (EPE). The disease typically occurs in young horses, with those between 4 and 9 months of age being particularly susceptible. *Lawsonia intracellularis* can cause a spectrum of clinical signs in foals, ranging from very mild to severe. Reported signs include ill thrift, lethargy, rough coat appearance, fever, weight loss, colic, and diarrhoea. Another common feature is oedematous, fluidy swelling of the lower limbs and beneath the abdomen. The presence of characteristic clinical signs in a young horse, combined with the detection of low albumin and protein on blood evaluation, and thickening of the small intestine detected on ultrasound examination, are highly suggestive of a *Lawsonia* infection.

Parasitic Infection

The majority of foals that are infected with *Strongyloides westeri* remain completely asymptomatic. However, clinical signs can develop when heavy burdens occur (Brown et al 1997). One study reported a case associated with diarrhoea where more than 2000 worm eggs per gram of faeces were detected (Netherwood et al, 1996). The primary source of infection for the foal is transmammary transmission of larvae via ingestion of the mare's milk. Ivermectin administration to the dam shortly after foaling can prevent transmission to the foal. *Cryptosporidium parvum* has been identified in the faeces of foals with diarrhoea, primarily in those less than 1 month of age. It was previously considered a pathogen of immunocompromised foals, either alone or as a co-infection (Netherwood, et al, 1996; Cole et al, 1998; Grinberg et al, 2008; 2009; Slovis et al, 2010). However, more recently it has been associated with sporadic disease and outbreaks in immunocompetent foals, either alone or as a co-infection (Cole et al, 1998; Grinberg et al, 2003). Treatment is generally symptomatic and strict biosecurity is required because of the contagious and zoonotic nature of the disease. Other protozoa, such as *Giardia*, have been identified in both healthy foals and those with diarrhoea. However, their role in the development of disease remains poorly understood.

Diagnostic investigations

A thorough history and clinical examination should always be performed and baseline blood work should be obtained (including a complete blood count and biochemistry profile). Further laboratory testing is dependent on the age of the foal and severity of clinical signs, and may include blood gas analysis, electrolytes and immunoglobulin concentrations. Blood cultures should also be performed if available, particularly in neonates or foals with a high suspicion of sepsis.

Establishing a diagnosis of diarrhoea is usually straight forward, but determining the specific aetiology can be more challenging. Although treatment in many cases is symptomatic, the underlying aetiology is particularly relevant from a biosecurity point of view and it is important to rule out the common infectious causes of diarrhoea. Faecal testing is recommended and tests should be based on the most likely causative agent in that particular age group. Options for testing are summarised in *Table 2*.

It has been demonstrated that in many foals with diarrhoea, more than one pathogen can be involved (Slovis et al, 2014). Therefore, a faecal panel (testing for a group of infectious agents most likely to affect a particular age group) is useful for the detection of co-infections. It is important to recognise that a positive test does not always confirm that the particular agent is the underlying cause of the diarrhoea, as several pathogens can be found in healthy foals as well.

Abdominal ultrasound should be performed in foals with diarrhoea to evaluate intestinal contents, wall thickness or detect evidence of ileus. Imaging of the liver and kidneys should be included in the assessment, in addition to umbilical structures in younger foals. Abdominal radiography can be used to identify the presence of sand or gas accumulations.

Management of foals with diarrhoea

Supportive care provides the mainstay of treatment in foals with diarrhoea. It is important that treatment is initiated promptly and should be re-evaluated frequently in response to clinical progression, particularly in neonates that are susceptible to rapid deterioration.

Fluid therapy

In foals with evidence of hypovolaemia, fluid resuscitation is required. In mildly affected foals (with no evidence of reflux or abdominal distension), enteral administration of fluids may be sufficient. However, in most cases, intravenous fluid therapy is required. Crystalloids, colloids, or a combination of both are commonly used. The rate, volume and type of fluid administered depends on the degree of hypovolaemia, cardiovascular status and plasma protein concentration. A common method of providing initial fluid resuscitation is to administer a balanced crystalloid solution (such as Lactated Ringers) as an intravenous bolus of 10–20 ml/Kg over 20–30 minutes, and then repeat as indicated by response to therapy. Foals are not tolerant of large sodium loads, so hypertonic saline is rarely a suitable choice for resuscitation (Magedesian, 2015).

Frequent reassessment should be performed and used to guide fluid therapy. This should include clinical examination, urine specific gravity, total protein, packed cell volume and lactate concentration, in addition to monitoring of ongoing losses. Excessive fluid volumes are also poorly tolerated in foals, so it is essential to provide sufficient support whilst avoiding fluid overload.

The administration of colloidal therapy can involve either natural or synthetic colloids. The use of hyperimmune plasma not only provides plasma proteins but also provides valuable immunoglobulins. This is essential in foals with failure of passive transfer, but also in compromised foals that can rapidly consume immunoglobulins despite initially adequate concentrations. In human medicine, the use of synthetic colloids such as Hetastarch has been associated with the development of coagulopathies, renal failure and an ultimately worse outcome, so their use has been questioned. A recent retrospective study comparing synthetic versus natural colloids in adult horses with enterocolitis suggested that survival of adult horses receiving natural colloids was improved, compared with horses receiving synthetic colloids (Kopper et al, 2019).

Table 2. Commonly used tests for infectious causes of diarrhoea

Infectious Agent	Commonly Used Tests
Rotavirus	Faecal enzyme-linked immunosorbent assay or polymerase chain reaction
Salmonella	Faecal culture or polymerase chain reaction Because of intermittent shedding is it recommended to perform multiple daily consecutive faecal samples (ideally 3-5).
Clostridium difficile and *Clostridium perfringens*	Polymerase chain reaction or enzyme-linked immunosorbent assay to detect toxins
Cryptosporidium	Faecal polymerase chain reaction or enzyme-linked immunosorbent assay
Equine Coronavirus	Faecal polymerase chain reaction
Lawsonia intracellularis	Faecal polymerase chain reaction (some foals stop shedding early in the course of disease so false negatives can occur. Also if the foal is sampled after antimicrobial treatment has been initiated then false negative results may occur). Serology can also be useful to confirm exposure to Lawsonia intracellularis
Strongyloides Westeri	Faecal worm egg count
Rhodococcus Equi	Faecal polymerase chain reaction (although diagnosis is problematic because Rhodococcus Equi can be detected in the faeces of healthy foals)

Electrolyte imbalances and acid-base disturbances are common in foals with diarrhoea and where possible should be monitored closely. Correction of these disturbances is crucial for recovery and is typically performed via intravenous fluid therapy. Attention must be paid to the rate of correction and rapid increases, particularly in sodium concentration, should be avoided. In more mild cases oral supplementation of electrolytes and bicarbonate may be sufficient.

Antimicrobials

Broad spectrum antimicrobials are recommended in neonatal foals with diarrhoea, because of the high likelihood of bacteraemia occurring secondarily to intestinal bacterial translocation (Hollis et al, 2008). Commonly used antimicrobials include the combination of amikacin (25–30 mg/kg every 24 hours, intravenous or intramuscular) and ampicillin (20 mg/kg every 6–8 hours, intravenous or intramuscular), or ceftiofur (5–10 mg/kg, every 6–12 hours, intravenous, intramuscular or subcutaneous). Consideration should be given to hydration status and renal function prior to starting any potentially nephrotoxic antimicrobials.

In cases with confirmed or suspected clostridial infection, metronidazole should also be administered. Pharmacokinetic studies indicate that for foals less than 10 days of age metronidazole should be administered at a rate of 10 mg/Kg, orally or intravenously, every 12 hours. For foals greater than 10 days of age, the dose is increases to 15 mg/Kg, administered orally or intravenously, every 12 hours. (Swain et al, 2015). In foals with significant intestinal disease, intravenous metronidazole should be used. Other conditions that require specific antimicrobial treatment include

KEY POINTS

- Diarrhoea is one of the most common clinical complaints in foals and can be associated with significant morbidity and mortality.
- Faecal testing is commonly performed to try and establish the underlying aetiology, however identifying a specific cause can be challenging.
- Foals can deteriorate rapidly, so they should be examined and treated promptly. This is particularly important if they show signs of dehydration, systemic inflammatory response syndrome, sepsis, colic, abdominal distension, depression, or if they have profuse or haemorrhagic diarrhoea.
- Treatment is often symptomatic and includes fluid therapy, antimicrobials, ulcer protection and analgesia.
- Many causes of diarrhoea in foals are highly contagious and strict biosecurity is essential to prevent the spread of disease.

Lawsonia intracellularis and *Rhodococcus equi*. A common antimicrobial choice for treating *Lawsonia intracellularis* is oxytetracycline (5-10mg/kg intravenously, every 12 hours). Treatment of *Rhodococcus equi* enterocolitis is similar to pulmonary *Rhodococcus equi* infection and includes the use of a macrolide combined with rifampacin, for example clarithromycin (7.5 mg/kg orally, every 12 hours) and rifampacin (10 mg/kg orally, every 12 hours).

Gastric ulcer therapy

The prophylactic use of anti-ulcer mediation is controversial. The benefit of prophylaxis is unproven and the incidence of gastric ulceration in one institution appeared to be unrelated to administration of ulcer prophylaxis (Barr et al, 2000). Furthermore, a multicentre study also found the use of proton pump inhibitors has been associated with the development of diarrhoea in hospitalised foals (Furr et al, 2012). However, foals with diarrhoea are at increased risk of developing gastric ulcers. A common approach is to use sucralfate, which has a number of advantages including increasing mucosal blood flow, and mucus and bicarbonate secretion.

Analgesia

Foals with enterocolitis may show mild to severe signs of colic, likely associated with inflammation or distension of the intestinal tract. Analgesia can be provided using butorphanol, lidocaine (continuous rate infusion), or non-steroidal anti-inflammatory drugs (NSAIDs) such as meloxicam. Because of their deleterious effects on prostaglandin production and the potential impact of this on intestinal epithelial health and renal function, NSAIDs should be used judiciously and only if absolutely necessary, particularly in foals with evidence of hypovolaemia.

Nutrition

Foals with severe diarrhoea, signs of colic or abdominal distension will often benefit from an initial period of milk withdrawal. In the hospital setting this is done by placing the foal in a cage, or with the use of a muzzle if possible. Evidence from human medicine would suggest that return to at least a small amount of enteral nutrition as soon as possible is preferred in order to provide the enterocytes with nutrition. If ongoing milk withdrawal is required (more than 24 hours) then it is essential to provide some form of parenteral nutrition (partial or total). This is frequently required in foals with colic, abdominal distension or evidence of reflux. It is important that the mare is milked regularly (every 2 hours) while the foal is being withheld. If lactose intolerance is suspected, then oral supplementation with lactase can be beneficial. Foals with mild diarrhoea and no evidence of colic or abdominal distention should continue to nurse.

Additional therapies

Intestinal protectants such as bismuth subsalicylate (Pepto-Bismol), and intestinal adsorbents such as di-tri-octahedral smectite (Biosponge), are commonly used in foals with diarrhoea. There has been little investigation into these products, but there is some evidence suggest that Biosponge may have some beneficial effect in reducing the absorption of clostridial toxins (Weese et al, 2003). In cases of sand colitis, treatment with psyllium is recommended. Probiotics have previously been suggested in the management of diarrhoea, in an attempt to restore a healthy intestinal microbiome. There has been limited work evaluating the use of probiotics in horses, although two large scale studies demonstrated that the use of probiotics in foals was significantly associated with the development of diarrhoea (Weese et al, 2005; Schoster et al, 2015). Therefore, until more research is available, the use of probiotics is not recommended in foals.

Biosecurity

Because of the potentially infectious nature of diarrhoea, strict biosecurity protocols should be implemented. This should include the use of separate equipment, boots and coveralls, foot dips, gloves and frequent hand washing. The exact disinfectant necessary for regular use depends on the causative organism.

Conclusion

In summary, management of foals with diarrhoea depends on the severity of the clinical signs. Foals with mild diarrhoea that are otherwise healthy often resolve spontaneously to with minimal medical intervention. Foals that show evidence of dehydration, systemic inflammatory response syndrome, sepsis, colic or abdominal distension, depression, or those that have profuse or haemorrhagic diarrhoea, should be examined and treated promptly. These foals can deteriorate rapidly and often require intensive care and management. Treatment is generally symptomatic and strict biosecurity protocols should be implemented to try and control the spread of disease.

Conflicts of interest

The author declares no conflicts of interest.

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