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Diarrhea in the foal

Foal heat diarrhea

J Freestone

INTRODUCTION

Foal heat diarrhea is experienced by 75–80 per cent of normal foals. Foal heat diarrhea, as the term implies, occurs in foals from 6–14 days of age and coincides with the first estrus cycle in the post-partum mare. This appears to be coincidental as foals separated from their dams and fed a controlled diet will still develop diarrhea at the same age. The cause of foal heat diarrhea has been widely debated with strongyloidosis and changes in milk composition largely eliminated as possible causes. From the work of Masri *et al.* (1986) it appears that the diarrhea results from a physiological change within the gastrointestinal tract as the foal develops a normal bacterial flora.

CLINICAL SIGNS

Foal heat diarrhea is most commonly a mild diarrhea that is malodorous and self limiting over a 7-day period. In a small number of foals the diarrhea may be profuse and may be prolonged, or it may initially resolve and then reoccur for an additional 2–3 days. The odor of diarrhea caused by rotavirus can often be distinguished from that of foal heat diarrhea. Foals show no adverse clinical signs with foal heat diarrhea, and remain bright, alert and responsive, afebrile, and they continue to suckle. The diarrhea 'scalds' the perineal area resulting in hair loss.

DIAGNOSIS

The diagnosis of foal heat diarrhea relies on the clinical signs presented by the foal. Routine hematology and biochemistry is normal. Foal heat diarrhea needs to be differentiated from other infectious causes of diarrhea including nutritional causes, viral diseases, and salmonellosis. On a large Thoroughbred stud the most likely differential diagnosis is rotavirus diarrhea. A good rule of thumb is to monitor the foal's nursing behavior and the size of the mare's mammary glands – foals with foal heat diarrhea will rarely go 'off suck' in contrast to foals with infectious causes of diarrhea.

TREATMENT

There is no treatment necessary for foal heat diarrhea as the condition is self limiting. The foal's perineal area can be cleaned and protected from scalding with the application of petroleum jelly or zinc oxide. If the foal deteriorates or the diarrhea is prolonged another cause for the diarrhea should be considered and the use of anti-ulcer medications, intestinal protectants, antibiotics, and fluid therapy considered.

Viral diarrhea in foals

TD Byars

INTRODUCTION

Foals are most susceptible to viral diarrheas during the neonatal, perinatal, and suckling periods by virtue of

being immunologically naïve. The causative or associated viruses include

- equine herpesvirus Type-1 (EHV-1)
- adenovirus
- coronavirus
- equine viral arteritis (EVA)
- rotavirus
- parvovirus
- viral infections that have not been completely identified but noted on fecal electron microscopy.

Most viral diarrheas are considered to be highly infectious and are rarely diagnosed at the time the symptoms are present. The exception is rotavirus, the most commonly recognized viral gastroenteritis in foals that is readily diagnosed by ELISA testing. Viral diarrheas should be suspected whenever an outbreak of foal diarrhea is present and routine microbiology is non-diagnostic. Viral diarrhea can be diagnosed by

- ELISA (rotavirus A)
- electron microscopy of tissues and feces
- polymerase chain reaction testing and immunoperoxidase (EHV-1)
- virus isolation from fecal or tissue samples obtained at post-mortem examination.

Unlike food animals where sacrifice to confirm a diagnosis may be elected, foals represent a population of companion animals where viral infections may be suspected but not confirmed, since the time involved in treatment can compromise ante-mortem diagnosis and post-mortem viral isolation. Koch's postulates are rarely documented in identifying viral causes of enteritis in the equine species.

CLINICAL SIGNS

Often viral diarrheas can not be differentiated from bacterial diarrheas since incubation periods may be similar and the clinical presentation can vary from acute to moderate severity, dependent upon the degree of insult and age of the foal. Clinical signs can vary from slight – a febrile foal that is not nursing, to profound – profuse watery to lightly hemorrhagic diarrhea accompanied by colic. The diarrhea can be fetid, and vary in color and consistency. In some cases atypical enteritis may be present in that the clinical assessment and blood values are consistent with enteritis but diarrhea is not present at the time of examination. Colic caused by enteritis may be difficult to differentiate from a surgical colic if blood values are reasonably normal and fever is not present (see Chapter 22). Abdominal pain associated with the early stages of viral enteritis can be severe, with tympany and occasionally gastric reflux. Further clinical diagnostic procedures are indicated in these cases with ultrasound examination being the diagnostic method most useful to rule out intussusception, volvulus, torsion, or peritonitis. A percentage of enteritic foals are unresponsive to analgesics and cannot be differentiated from surgical cases until tympany has been relieved by the use of prokinetics or, more rarely, percutaneous trocarization. Trocarization is usually contraindicated wherever surgical options are available since foals should be considered more susceptible to secondary peritonitis than adults.

TREATMENT

Treatments for viral diarrheas are generally empirical and symptomatic

- fluid and electrolyte therapy
- plasma
- antibiotics
- anti-ulcer therapy
- anti-diarrheal medications
- analgesics
- antipyretics

Precautionary antibiotics and anti-ulcer medications (see Chapter 23) should be prescribed. Fluid therapy, oral or parenteral, for maintenance of normal hydration is the main objective of treatment. Fluid therapy is necessary to correct dehydration, shock, and electrolyte imbalances. In some cases colloids (plasma, albumin, or hetastarch) may assist in the intravascular retention of crystalloid (fluid) therapy. Other treatments include the use of antidiarrheal medications, analgesics, and antipyretics. The fluids and colloids selected are based on laboratory findings, electrolyte and acid–base imbalances, and clinical signs. Oral supplementation should include access to fresh and electrolyte water, and a salt block. Potassium deficits can be corrected in intravenous fluids at a rate of 0.5 mEq kg^{-1} h^{-1} or orally as potassium chloride in the form of 'lite' salt mixed with yogurt. Patients with reflux, ileus, or extreme cachexia may benefit from the initiation of total parenteral nutrition (with or without lipids). Antidiarrheal medications are rarely effective in altering the course of the diarrhea but medications such as bismuth subsalicylate and kaolin may help reduce bowel inflammation and provide for secondary toxin absorption and resorption when combined with activated charcoal. Oral plasma from adult donors has been used in cases of viral diarrhea in foals with questionable efficacy. Analgesic use in viral diarrheas should emphasize the discriminating use of ulcerogenic non-steroidal anti-inflammatory drugs

(NSAIDs). Dipyrone is not currently available commercially but has provided excellent analgesia in mild colic, along with its anti-pyretic activity, in foals with diarrhea of various causes. Intravenous and intramuscular butorphanol (in small animal dilutions) is useful in the control of colic without cardiovascular or ulcerogenic side effects. Xylazine may also be used to control colic but temporarily affects cardiovascular function and potentiates ileus.

ROTAVIRUS AND SIMILAR VIRAL INFECTIONS

Rotavirus diarrhea is considered to be species specific but may involve variant strains in foals. Exposure is from carrier adults, infected foals, and mechanical transmission by humans and fomites. The incubation period is 1–2 days and it is highly infectious to suckling foals of any age. The pathogenesis of infection primarily involves the intestinal epithelial cells. Villi become shortened or denuded, crypts become hyperplastic, and the ensuing diarrhea is combined secretory and malabsorptive enteritis. Additionally carbohydrate enzymes and lactose become deficient. The diarrhea, if present, is usually watery and distinctly fetid. Diagnosis is by ELISA testing or electron microscopy of feces for viral particle identification. Treatment is non-specific and the virus can be shed for approximately 5–7 days after the diarrhea has resolved. Medications containing lactase have been used to improve digestion of milk lactose, but the efficacy of this treatment remains unproven. A commercial modified live virus vaccine is currently available for use in mares prior to foaling to accentuate colostral antibodies. Foals from vaccinated mares can still become infected with rotavirus although the clinical signs may be attenuated.

In Ireland and central Kentucky a unique cyclic epizootic of a suspected form of rotavirus diarrhea was noted in 1987 and 1995, nicknamed the 'pink-rosewater diarrhea' or '36-hour scours'. The disease was highly infectious with virtually every foal at respective farms being clinically affected within 36 hours of birth. The clinical signs include a pinkish watery diarrhea, relatively non-fetid, usually complicated by dehydration and colic associated with abdominal tympany. Colics were often severe and unresponsive to analgesics. Neostigmine used to relieve tympany was most effective in the resolution of colic. Often treatments were empirical or symptomatic. Routine sanitation procedures, including pressure washings and disinfection, were ineffective. Washings and disinfection of the mares' udders were also ineffective. Foaling in paddocks or pens outside the barn environment resulted in a dramatic cessation of new clinical cases. Viral particles were noted on fecal electron microscopy without a definitive identification of the causative viral etiology.

PROGNOSIS

The prognosis for foals with viral diarrhea is usually favorable with fluid therapy and supportive care. Secondary complications with bacterial infections or the gastric ulcer syndrome can reduce the number of favorable outcomes. Foals having survived viral diarrhea are usually immune to subsequent infections, although rotavirus is known to recur occasionally, albeit with reduced clinical severity.

Salmonellosis in the foal

JL Whiting and TD Byars

INTRODUCTION

Salmonella spp. are the most commonly diagnosed causative agents of bacterial enterocolitis in the adult equine, and has been reported as the most common cause of bacterial diarrhea in the foal. In foals less than 14 days of age, Salmonella infections can lead to bacteremia, septicemia, septic shock, and death, with diarrhea occurring secondarily. Other bacteria, including *Actinobacillus equuli, Escherichia coli, Streptococcus* spp. and *Klebsiella* spp. may also cause diarrhea secondarily to septicemia.

Young and immunocompromised animals are more susceptible to Salmonella infections, in that exposure to a lower dose of the organism can result in infection. This increased susceptibility of the young may in part be because of a less sophisticated or less well established microflora within the gastrointestinal tract. Experimental data have shown the significance of normal gastrointestinal flora in restricting the ability of the Salmonella organism to establish and proliferate within the intestine.

The most common source of exposure and infection in the foal is another horse. Often the mare herself is an asymptomatic carrier, shedding the organism during the stress of parturition and exposing the foal to the pathogen *in utero* or in the post-foaling environment.

PATHOGENESIS

Salmonella spp. are gram-negative, facultative, anaerobic bacteria, which usually gain access to the gastrointesti-

nal tract via the fecal–oral route. The bacteria must combat a number of non-specific host defense mechanisms – gastric acidity, normal intestinal flora, peristalsis, intestinal mucus, lactoferrin and lysozyme secretions within the gastrointestinal tract – in order to establish infection. Salmonella organisms have many virulent properties enabling them to establish infection within the host. Among these are flagellar and chemotactically directed motility, capsular and surface antigens, macrophage-induced proteins, endotoxin, enterotoxin, cytotoxin, plasmids, and iron-chelating enzymes. Once Salmonella organisms come in close proximity to, or possibly in contact with, the brush border of enterocytes, the microvilli and tight junctions undergo degeneration. Flagellar motility may enable the organism to approach enterocytes close enough for adhesion to occur. Surface O antigens and fimbriae may then facilitate adherence of the bacteria to the host receptor cells.

The bacteria migrate through the enterocyte and access the lamina propria where their presence stimulates an inflammatory response. The macrophages and neutrophils recruited will phagocytize the bacteria, and it is within these phagocytic cells that Salmonella organisms survive and multiply, while remaining protected from antibiotics, antibodies, and complement. Flagella are thought to protect the organism from intracellular killing, while macrophage-induced proteins produced by *Salmonella* spp. have been shown to block fusion of the phagosome and lysosome, allowing intracellular survival and multiplication.

Both phagocytized and free Salmonella organisms travel via the lymphatics to regional lymph nodes where they persist in stimulating an inflammatory response. From here the bacteria continue via efferent lymphatics to drain into the blood circulation. Once in the circulation, the bacteria are generally cleared via the reticuloendothelial system, primarily through the liver and the spleen. Septicemia and its sequelae (more common in the neonate than the adult) can occur if the infection is not contained by the mononuclear phagocytic system. Immunity against *Salmonella* spp. requires both cell-mediated and humoral immunity as the bacteria are intracellular pathogens. The neonate's 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.

Inflammation within the bowel wall results in villus blunting and degeneration and abnormal extrusion of enterocytes. Cytotoxins may in part be responsible for cellular destruction by inhibiting protein synthesis. The diarrhea in the disease process of Salmonella infections is a result of malabsorption because of this destruction of epithelial cells. Additionally, enterotoxins may induce secretion of fluid from intact intestinal epithelial cells.

Lipopolysaccharide (LPS), or endotoxin, is a component of the outer membrane of gram-negative bacteria, and contributes greatly to the pathogenesis of salmonellosis. Endotoxin activates a variety of host cells (platelets, macrophages, endothelial cells, leukocytes) and host tissues to release inflammatory mediators such as arachidonic acid metabolites, prostaglandins, leukotrienes, tumor necrosis factor, interleukins, granulocyte and macrophage stimulating factor, and reactive oxygen radicals. LPS can also stimulate both the intrinsic and extrinsic clotting cascades and activate complement by the classical and alternative pathways. Endotoxemia leads to alterations in hemodynamics, homeostasis, metabolism, and endothelial integrity, resulting in tissue injury, vascular collapse, and multiple-organ system failure (see Chapter 11).

CLINICAL SIGNS

Clinical signs of salmonellosis are variable and can range from mild enteritis to fulminating septicemia (Table 27.1).

Manifestations are attributed to enterocolitis, septicemia, and endotoxemia. Early in the course of the disease, fever, decreased nursing, and depression are commonly found. Neonates can present with hypothermia. Foals frequently show signs of moderate to marked abdominal pain and can have associated abdominal distension. Other differential diagnoses must be considered in the neonate as colic symptoms may accompany mechanical gastrointestinal obstruction, for example meconium impaction, intussusception, volvulus, and colon torsion (see Chapter 22). Ileus often occurs, contributing not only to colic and distension, but also to decreased or absent normal progressive motility

Table 27.1. Clinical signs of salmonellosis in foals

Pyrexia
Depression
Decreased nursing
Abdominal pain
Abdominal distension
Ileus
Dehydration
Congested mucous membranes
Prolonged capillary refill time
Diarrhea

sounds. Fluid and gas sounds are frequently appreciated when auscultating the abdomen. Dehydration, as evidenced by decreased skin elasticity, dry mucous membranes, and sunken eyes, can become severe with ongoing fluid losses that may lead to poor tissue perfusion. Endotoxemia contributes to decreased perfusion by stimulation of various inflammatory mediators (thromboxanes, prostaglandins, leukotrienes, and catecholamines) which can cause both vasoconstriction and hypotension. Clinically, vasoconstriction is seen early in the course of endotoxemia and is represented by pale mucous membranes, whereas decreased vascular tone appears as muddy, dark-red, congested mucous membranes with a toxic line along the gingiva. Additional findings associated with poor perfusion include tachycardia, elevated pulse rate and intensity, prolonged capillary refill time, cold extremities, and depressed mentation.

Clinical signs of bacteremia may manifest as infections evident in other organ systems such as

- pneumonia
- septic arthritis
- uveitis
- osteomyelitis
- skin abscesses
- meningitis
- nephritis.

Severe septicemia can lead to septic shock, multiple organ system failure, and circulatory collapse.

Diarrhea may not be present initially and neonates may die rapidly from severe septic shock before diarrhea develops. Diarrhea associated with acute Salmonella enterocolitis is most often profuse and liquid with little solid material present. Flecks of blood may rarely be present. Foals will defecate in increased frequency and volume. Colic and straining during defecation are common features associated with the high volume of diarrhea produced, while rectal prolapse can occur.

CLINICAL PATHOLOGY

Although not diagnostic for the disease, the most consistent hematological abnormalities found with severe Salmonella diarrhea infections are

- leukopenia
- neutropenia with a degenerative left shift
- toxic changes (cytoplasmic vacuolation and toxic granules) seen in granulocytes.

An inversion of the neutrophil:lymphocyte ratio can indicate sepsis. A rebound neutrophilic leukocytosis may occur later in the course of disease, sometimes indicating recovery. Thrombocytopenia can be found in some cases. Fibrinogen can be variable, with low (< 100 mg/dl) values being attributed to coagulopathy and elevated (> 1000 mg/dl) values being attributed to inflammation. Hematocrit is generally markedly increased because of hemoconcentration and splenic contraction. Total plasma protein is initially quite elevated because of hemoconcentration, but will decrease, along with serum albumin levels, with ongoing enteric losses secondary to mucosal damage or generalized endothelial damage. Many neonates will have decreased serum immunoglobulin G (IgG) levels because of protein catabolism commonly associated with septicemia. Foals that experience a failure of passive transfer (FPT) are predisposed to septicemia, and it can be hard to differentiate if the low IgG led to septicemia or if it was a result of septicemia.

Electrolyte and acid–base imbalances can be profound with Salmonella enterocolitis and commonly include

- hyponatremia
- hypokalemia
- hypochloremia
- hypocalcemia
- metabolic acidosis.

Hypoglycemia in foals may be marked as a consequence of decreased glycogen stores in the liver and bacterial depletion due to sepsis. Azotemia is usually prerenal in origin, but can be caused by acute renal failure or bacterial nephritis in profoundly dehydrated, endotoxemic, or septicemic animals. Hepatic enzymes may be mild to moderately increased as a consequence of absorption of bacterial toxins (endotoxins). Endotoxin-mediated lactic acidosis can result from poor perfusion. Mediators of inflammation stimulated by endotoxemia can lead to a hypercoagulable state followed rarely by disseminated intravascular coagulation (DIC), as evidenced by prolonged prothrombin time, partial thromboplastin time, depletion of antithrombin III and increased fibrin degradation products.

DIAGNOSIS

Diagnosis of *Salmonella* spp. as the causative agent of diarrhea is demonstrated by a positive fecal culture, while a positive blood culture is needed to diagnosis Salmonella septicemia. Isolation of the organism from fecal material is variable as *Salmonella* spp. may be intermittently shed in the feces. With acute enteritis, the feces can have little solid material and the chance of culturing the bacteria is diminished (although better

than in adult horses). A minimum of three to five consecutive 1 gram fecal cultures taken 24 hours apart are recommended to increase the chance of isolating the organism. Fecal cultures from the mare should also be submitted to assist in determining the source of infection.

TREATMENT

Therapy for salmonellosis is aimed at maintaining hydration and electrolyte balance in the face of ongoing losses, reducing the effects of endotoxemia, preventing or treating bacteremia, and gastroprotectant therapy (Table 27.2).

Aggressive intravenous fluid therapy may be required as dehydration can rapidly become severe in the foal with enterocolitis, and effects of decreased intravascular volume can be profound. Electrolyte and acid–base abnormalities can be marked and serum parameters should be monitored frequently to maintain balance. Isotonic fluids are routinely used to restore and maintain hydration status, with additional electrolytes, for example potassium and bicarbonate, added as indicated by deficits found in serum chemistry analysis. Potassium chloride should not be administered at a rate greater than 0.5 mEq kg^{-1} h^{-1} in the foal. In the severely affected foal with poor perfusion, signs of septic shock or reduced plasma oncotic pressure (hypoproteinemic: <4.0 mg/dl or 40 g/l; hypoalbuminemic: < 1.8 mg/dl or 18 g/l; and hemoconcentrated with ventral or distal limb edema), colloids such as hydroxyethyl starch, at a dose of 10 ml/kg, can be beneficial. Intravascular volume can be expanded, and vascular perfusion and oncotic pressure improved with a decrease in interstitial fluid accumulation. Colloids are generally followed by continued crystalloid fluid therapy. When used in conjunction with colloids, a decreased amount of crystalloid fluids are required. Plasma is recommended in the hypoproteinemic foal with hypoalbuminemia and/or low IgG levels. In addition, plasma contains coagulation factors and antithrombin III, which could benefit the endotoxemic patient. Hyperimmune plasma containing immunoglobulin-recognizing LPS core antigen has been recommended in horses with Salmonella infections at a dose of 0.4 ml/kg. Fluids containing dextrose (5% solution) or oral supplementation via a nasogastric tube may be required in the foal that has stopped nursing. Alternatively, the catabolic patient may benefit from oral supplementation with high-nitrogen oral solutions (osmolite), partial parental nutrition (PPN) or total parental nutrition (TPN).

Table 27.2. Treatments for salmonellosis in foals

- Intravenous fluid therapy
  - Isotonic fluids
  - Bicarbonate
  - Potassium chloride
  - Colloids
  - Plasma
  - Hyperimmune plasma
  - Dextrose
- Partial or total parenteral nutrition
- Antibiotics
- Polymyxin B
- Flunixin meglumine
- Pentoxifylline
- Bismuth subsalicylate
- Activated charcoal
- Live yogurt
- Anti-ulcer therapies

Although antibiotic therapy will not alter the course of the diarrhea or reduce the incidence of shedding of the Salmonella organism, it is recommended that foals with Salmonella infections be treated with antibiotics in the hope of preventing bacteremia and to treat any sites of secondary infection. Appropriate antibiotic therapy should be established based on sensitivity results of fecal or blood cultures. Ideally lipid-soluble antibiotics such as trimethoprim-sulfonamides and chloramphenicol, should be used as the Salmonella organism survives intracellularly. Often the *Salmonella* spp. isolated, especially in nosocomial infections, will be resistant to the aforementioned antibiotics, and other broad-spectrum choices such as third generation cephalosporins or penicillin and aminoglycoside combinations are found to be more effective. Antibiotics may contribute to the release of endotoxins in cases of rapid bacterial death. For this reason patients can be treated with medications that decrease the effects of circulating endotoxin prior to initiation of antimicrobial therapy. Polymyxin B, at a low dose of 6000 IU/kg, binds and removes endotoxin from circulation. Cyclooxygenase inhibitors such as flunixin meglumine (0.25 mg/kg i.v. t.i.d.) will both ameliorate the effects of endotoxemia by decreasing synthesis of prostaglandins and thromboxanes, and decrease the secretory component of diarrhea by blocking prostaglandin-mediated hypersecretion of enterocytes. Non-steroidal anti-inflammatory drugs should be used cautiously in foals because of the greater risk of gastroduodenal ulcers. Pentoxifylline (7.5 mg/kg p.o. b.i.d.) has been shown to reduce endotoxin-induced synthesis of tumor necrosis factor, a contributor to endotoxemia associated with sepsis. In addition, pentoxifylline increases red blood cell deformability,

decreases blood viscosity, decreases platelet aggregation, and decreases thrombus formation, thereby combating conditions contributing to impairment of regional blood flow.

Bismuth subsalicylate is commonly used as an intestinal protectant. The bismuth is thought to have anti-endotoxic and weak antibacterial properties while the salicylate has antiprostaglandin activity which may decrease enterocyte hypersecretion. Activated charcoal and/or mineral oil can be used to decrease absorption of endotoxin. Yogurt or other lactobacillus-containing products can be used to help reintroduce beneficial flora to the gastrointestinal tract.

Anti-ulcer medication is routinely recommended and administered prophylactically and therapeutically to ill foals because of their predisposition to gastric ulcer syndrome. Omeprazole (a gastric acid (proton) pump inhibitor), or famotidine, ranitidine, cimetidine (H_2 antagonists), and sucralfate (a cytoprotective agent) are commonly used medications. It is interesting to recall that one important host barrier to Salmonella infections is the ability of acidic pH in the stomach to prevent live bacteria from gaining access to the intestine. Changing gastric pH with anti-ulcer medication may in fact enhance infection.

PREVENTION AND CONTROL

The Salmonella organism is relatively prevalent within the environment and can be shed in the feces of clinically normal horses. The most common route of infection is fecal–oral. The mare is often found to be shedding the organism and the foal has probably contracted it from her. Neonates are at greater risk during the first 24 hours of life as the organism may gain access via the gastrointestinal tract prior to gut closure. Overcrowding, improper sanitation, and inadequate umbilical care all put the neonate at risk for Salmonella bacteremia and consequent septicemia.

Adequate colostral antibody absorption is important to develop the foal's immune defense system. A serum IgG concentration of more than 800 mg/dl at 24 hours of age is recognized as optimal passive conference of immunity in the neonatal foal. This immunity is especially important in the neonate at risk for sepsis. Plasma transfusions with hyperimmune plasma from donors vaccinated against mutant strains of J-5 *Escherichia coli* or *Salmonella typhimurium* have been reported to provide IgG protection against gram-negative core antigens, but clinical response to this therapy is variable. In addition, plasma provides opsonins which improve the foal's immune function. Sick neonates can experience increased immunoglobulin consumption, possibly because of sequestering of IgG within the intravascular space or at sites of inflammation, and can benefit from plasma transfusions even if initial colostral absorption is adequate. Autogenous vaccines have been used to stimulate immunity against *Salmonella* spp., but approved and proper preparation is difficult.

Animals identified as infected with *Salmonella* spp. should be kept isolated from the general population until they culture negative. Both mares and foals should be cultured. Infected animals can continue to shed organisms in their feces intermittently for several days to weeks. Daily fecal cultures should be taken beginning at 4 weeks after the cessation of clinical signs, and three to five negative cultures are needed before putting the animal in contact with other foals can be considered.

Clostridial enterocolitis in foals

TJ Divers

Clostridial diarrhea has been diagnosed in foals at an increasing rate over the past 5 years. It is unclear if this is a result of increased prevalence of the disease or increased use of more sensitive diagnostic tests for intestinal clostridial toxins.

ETIOPATHOGENESIS

Clostridium perfringens type C is a well-proven cause of colic and diarrhea (often hemorrhagic) in young foals. The disease almost always occurs in foals less than 5 days of age that have received sufficient colostrum. Pancreatic trypsin is inhibited by a trypsin inhibitor in colostrum, which undoubtedly plays a role in the potential for *C. perfringens* colonization and increased toxin concentration in the foal's small intestine during the first week of life. *C. perfringens* type C produces a beta toxin which causes severe intestinal necrosis and hemorrhagic diarrhea. As the intestinal wall becomes damaged the organism can be found in the blood of many affected cases. In later stages of the disease the organism can be found in the peritoneal fluid. *C. perfringens* type C diarrhea can be either a farm problem or it can present as an isolated case. Foals, such as orphan foals, that may be given both colostrum and milk in unusually large amounts via a nasogastric tube may be at increased risk. Although unconfirmed, exposure to the organism may be via the mare rather than environmental contamination.

Clostridium perfringens type A has been incriminated as a cause of diarrhea in foals of all ages. Proof of the relationship between *C. perfringens* type A in the foal's stool, and diarrhea in foals has been difficult. As in adult horses, *C. perfringens* type A organisms are more common in foals with diarrhea than in healthy foals, but no toxin marker has been found in the foal that distinguishes a pathogenic strain of *C. perfringens* type A from non-pathogenic strains. *C. perfringens* type A enterotoxin and/or its enterotoxin gene can be found in both normal and diseased foals. *C. perfringens* type A may cause diarrhea in foals, but more research is needed to prove cause and effect. A similar situation exists with *C. difficile* and its relationship to foal diarrhea. *C. difficile* has been reported, and has frequently been incriminated as causing outbreaks of diarrhea in young foals (generally < 3 weeks of age). In these outbreaks there has been no history of prior antibiotic treatment to predispose the animals to the proposed *C. difficile* diarrhea. Proving cause and effect has been difficult since normal foals may have both *C. difficile* and its toxin in their stool. This situation is also well-known in children. It may be that *C. difficile* is a primary pathogen in some cases of foal diarrhea, or it may be present in the stool in greater numbers because of the diarrhea, or it may be acting with another pathogen to cause diarrhea. Other pathogens that may be present simultaneously include *Cryptosporidium* spp., *Bacteroides fragilis*, rotavirus type A, or a virus similar to rotavirus but smaller than type A.

CLINICAL SIGNS

Colic often precedes the diarrhea by a few hours and can be severe. Mild to moderate abdominal distension generally precede the diarrhea. There may be some reflux after passage of a soft nasogastric tube, but more commonly reflux is absent or minimal. Fever is often present. *Clostridium perfringens* type C generally causes a hemorrhagic enteritis with blood-stained diarrhea (Plate 27.1). Diarrhea associated with *C. difficile* or *C. perfringens* type A is more commonly brown and fetid.

DIAGNOSIS

The diagnosis of clostridial enteritis, or any enteritis in foals, should be based on signalment and historical information, for example age of the foal, clinical findings, fever, leukopenia, low serum sodium and chloride, liquid gut sounds on auscultation, in addition to fecal cultures and toxin assays. Radiographic examination, performed using 85 kVp and 20 mA with rare earth screen cassettes, is useful in distinguishing enteritis from surgical conditions, for example intussusception, in the colicky foal. Small intestinal obstructive lesions have a few distinct inverted U-shaped loops of bowel and there is less intestinal gas distension than with enteritis. Ultrasound examination of the abdomen using a 5-mHz probe is most helpful in differentiating between surgical disorders and enteritis as causes of abdominal pain. The small intestine of foals with enteritis is generally more hypoechoic than normal (Figure 27.1) and the motility may be increased. With strangulating diseases of the small intestine, motility of the distended intestine is usually absent. The ultrasound examination should be performed with the foal standing if possible.

Fecal cultures should be submitted for *Clostridium* spp. culture (anaerobic media) and toxin assay (*C. difficile* toxin A and B, and *C. perfringens* alpha and enterotoxin). For toxin assays, the sample should ideally be delivered immediately to the laboratory or the feces frozen and sent by overnight mail. An estimate of the number of *C. perfringens* organisms in the feces may be helpful in determining significance, but quantitative cultures require that a fresh sample (ideally taken from the rectum) be kept under anaerobic conditions and delivered immediately to the laboratory. Large numbers of *C. perfringens* (> 10^3 colony-forming units/ml of feces) would be supportive of the diagnosis. A gram stain of the feces is helpful in the diagnosis if there are

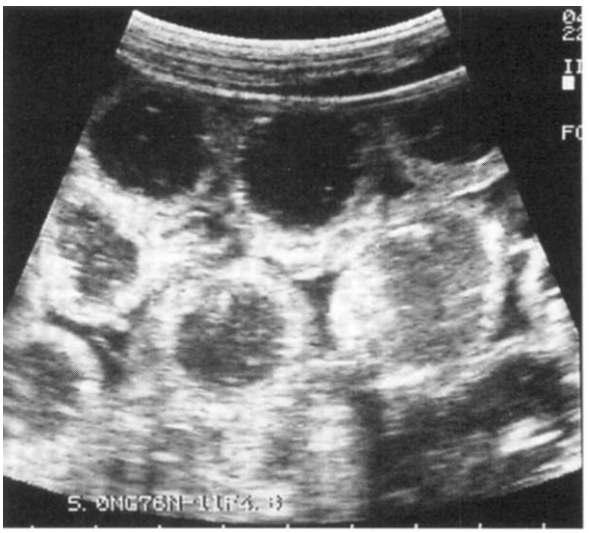

Figure 27.1 Ultrasonogram of the abdomen of a foal affected by clostridiosis showing multiple distended loops of small intestine with grossly thickened intestinal walls. In real time hypermotile movement of intestinal contents is evident, helping to differentiate enteritis from mechanical obstructions of the small intestine

a large number of gram-positive rods. Spores are more commonly seen with *C. difficile* and the organism can often be more curved in appearance and have a darker gram-positive stain than *C. perfringens*. Genotyping would be needed to determine *C. perfringens* type (A–E). Blood cultures should be performed on young foals (<1 week of age) with diarrhea as *C. perfringens* type C can often be found in the blood or peritoneal fluid in the later stages of the disease.

TREATMENT

Treatments that can be helpful for clostridial diarrhea are shown in Table 27.3.

Signs of abdominal pain should be controlled to minimize injury to the foal. Dipyrone (22–33 mg/kg i.v.) or butorphanol (4–6 mg/kg i.m.) can be used initially. Low doses of flunixin meglumine can be used sparingly. Foals with colic, ileus, and severe or progressive 'gaseous' abdominal distension that have been unresponsive to appropriate medical treatment and are believed *not* to have an obstructive disorder, can be given neostigmine (0.2–0.4 mg/foal s.c.) after sedation with xylazine in an attempt to evacuate the gas.

Lactated Ringer's solution should be given to reduce fluid deficits. Potassium chloride (20 mEq/l) should be added if the foal is hypokalemic, or if sodium bicarbonate and dextrose have been administered, and if the foal has been seen to urinate. Additional potassium is generally needed in foals having diarrhea for more than 2 days or in foals receiving large volumes of intravenous fluids. If the foal appears weak add 10 g dextrose/l unless the blood glucose concentration is normal. If the blood glucose is normal add 5 g/l. Bicarbonate should only be used if the acidosis is severe and/or persistent.

Two liters of plasma should be given intravenously (preferably the plasma should have antibodies against endotoxin, although the LPS antibodies may not be as important as some naturally occurring factors in plasma, e.g. anti-thrombin III). *Clostridium perfringens* type C and D antiserum can be given orally to affected foals. If the foal is in hypotensive shock and the plasma and polyionic fluids do not improve the condition (as determined by monitoring the blood pressure or by clinical impressions, e.g. poor capillary refill, severe and persistent tachycardia, and cold extremities), dobutamine (5–10 $\mu g\ kg^{-1}\ min^{-1}$) should be administered via a slow intravenous drip.

Antimicrobial therapy should include intravenous penicillin, 44 000 IU/kg i.v. q. 6 h, and amikacin, 18 mg/kg q. 24 h, (carefully monitor urine production, serum creatinine, and amikacin trough levels). Metronidazole, 10 mg/kg p.o. q. 12 h, may also be administered. Broad spectrum antibiotics are indicated as bacterial translocation to other organs can occur.

Ranitidine 1.5–2.2 mg/kg i.v. q. 8 h or famotidine 0.7–1.4 mg/kg i.v. once daily should be used in the hope of preventing gastric ulcers. Once the colic subsides, these or other H_2-blockers or proton pump blockers can be given per os.

Pepto bismol (56–112 g (2–4 oz) p.o. q. 4–6 h) with 28–56 g (1–2 oz) yogurt may be of some benefit in reducing toxin absorption and re-establishing normal intestinal flora. The foal can be allowed to nurse but should not be force-fed milk.

Table 27.3 Treatments for clostridial diarrhea

Analgesics	– dipyrone
	– butorphanol
	– flunixin meglumine
Neostigmine	
Lactated Ringer's solution	
Potassium chloride	
Dextrose	
Sodium bicarbonate	
Plasma	
Dobutamine	
Antibiotics	– penicillin
	– amikacin
	– metronidazole
H_2-blockers	– ranitidine
	– famotidine
Pepto bismol/yogurt	

PROGNOSIS

The prognosis with *Clostridium perfringens* type C is variable, intestinal necrosis rapidly occurs in a few cases with large numbers of the organism being identified in both blood and peritoneal fluid. Less severely affected cases respond dramatically to treatment and may appear normal within 2–3 days. *C. difficile* and *C. perfringens* type A-associated disease seems to produce a more protracted diarrhea. The prognosis for either infection is generally good if the foal is nursing at recognition of the disease, or if nursing is strong after 24 hours of treatment. Gastric ulceration, electrolyte imbalances, and cachexia may be significant problems in a few foals.

CONTROL

Clostridium perfringens type C diarrhea is often an isolated event on a farm requiring few control measures.

Cleaning the mare's udder prior to the foal nursing may be the most appropriate control measure and should be routinely recommended. *C. perfringens* type C toxoids are available but would not routinely be recommended for the pregnant mare unless the farm has a proven problem with *C. perfringens* type C. A more significant problem exists with farm outbreaks of foal diarrhea presumed to be associated with either *C. difficile* or *C. perfringens* type A. It may help to ensure cleanliness of the mare at parturition, disinfect the foaling area, and avoid using a common foaling stall. Prophylactic use of metronidazole, 10 mg/kg q. 12 or 24 h, from day 1 (do not administer prior to colostrum) to day 5 appears to be helpful in stopping outbreaks on some farms. *Lactobacillus acidophilus* probiotics may be administered for either prophylaxis or treatment but their efficacy is not proven. Hospitalized foals, either with or without diarrhea may be shedding *C. difficile* in the greatest numbers. Their stalls should be disinfected with an appropriate disinfectant (hypochlorite, glutaraldehyde, or phenolics), and all personnel entering and leaving the stall should wash hands and wear protective clothing and boots.

Rhodococcus equi as an agent of intestinal disease

KA Sprayberry

INTRODUCTION

Rhodococcus equi is a gram-positive, facultative intracellular aerobe, it is known primarily as a pathogen of the respiratory tract of the juvenile horse. The organism is a saprophytic inhabitant of the soil, favoring soils in warm climates where the manure of herbivores is present. Such soils promote survival and amplification of *R. equi* populations because molecules produced by fermentative digestion in the equine hindgut are growth factors for the organism. The typical manifestation of disease caused by this bacterium is an abscessing, pyogenic, granulomatous bronchopneumonia in foals aged 1–6 months, but many extrapulmonary manifestations of infection, including colitis and abdominal lymphadenitis, have been described.

Originally classed taxonomically in the genus *Corynebacterium*, the organism was reclassified as *Rhodococcus* spp. on the basis of genetics, chemistry, and ecology. Members of this genus are soil inhabitants, having in common the production of red pigment, but only *R. equi* has been reported as a pathogen in animals or humans. The organism is in the same taxonomic order (Actinomycetales) as mycobacteria. Mycobacteria, like *R. equi*, are primarily pathogens of the respiratory and intestinal tracts, causing pulmonary and intestinal tuberculosis in humans (*M. avium*, *M. bovis*, and *M. tuberculosis*) and Johne's disease, a chronic, granulomatous inflammation of the intestinal tract of ungulates (*M. paratuberculosis*). The tuberculous, pyogenic granulomas of mycobacteria infections are histologically similar to rhodococcal abscesses in their composition of infected macrophages and multinucleate giant cells with neutrophilic infiltration.

EPIDEMIOLOGY AND PATHOGENESIS

Because the bacterium resides endemically in types of soils which support populations of horses, it is an agent to which most, if not all, horses are exposed. The incidence of disease associated with *Rhodococcus equi*, however, varies. On some farms *R. equi* pneumonia is rare, while on others clinical disease occurs enzootically, even though the organism can be cultured from the soil of both. This incongruity is likely to be a result of differences in the type of soil, climate, prevalence of dusty conditions, stocking rate, and intensity of management that exist between farms, as well as differences in virulence among resident strains of the organism. Virulent strains of *R. equi* are characterized by the presence of a 15 or 17.5 kDa virulence-associated protein (VapA) on the cell membrane. Farms which have clinical disease due to *R. equi* are usually endemic premises for VapA strains of the organism, while farms having little incidence of disease are infected less heavily with the virulent organism. This protein is encoded for by an 85 or 90-kilobase plasmid. Though long recognized as an identifying marker for virulent strains, it has recently been shown conclusively that this plasmid is in fact a virulence factor for the organism. The presence of the plasmid is essential for intracellular replication within macrophages and subsequent development of disease. The organism dwells and replicates within phagosomes after being phagocytized by macrophages, preventing (by an unknown mechanism) the usual fusion of the phagosome with a lysosome. Macrophages thus infected do not undergo the respiratory burst associated with the lysosomal enzymatic activation which mediates intracellular killing. Infection of macrophage cells by *R. equi* eventually causes the degeneration and death of the immune cell, possibly by inappropriate lysosomal rupture and degranulation into the cytoplasm. Neutrophil cells of both foals and adult horses function as effective phagocytes, and can effectively process and destroy *R. equi*.

Inoculation of foals occurs via either the respiratory route, following inhalation of aerosolized particles, or the oral route, via ingestion. In dusty conditions, bacteria present in the soil and feces become aerosolized, serving as the direct source of exposure and pulmonary infection for foals. Colonization of the bowel by *Rhodococcus. equi* occurs when foals ingest infected soil or forage, are coprophagous, or swallow expectorated, bacteria-laden sputum. *R. equi* pneumonia is also prevalent in areas with grass pasture and little or no dust or exposed soil. In these circumstances, feces from adult horses serving as passive carriers may be an important source of exposure for foals. In adult horses, ingestion results in passive passage of the organism through the intestinal tract, with resultant deposition of the bacterium back into the environment. In immunologically naïve foals, however, the organism thrives and replicates, resulting in significant amplification of bacterial numbers in the environment and enhanced risk to other young stock if manure produced by infected foals is not promptly removed. During the optimal environmental conditions that prevail during summer months, *R. equi* numbers in contaminated soil can multiply by ten-thousand-fold in 2 weeks, such that 1 gram of soil could theoretically contain millions of virulent organisms.

CLINICAL SIGNS

The clinical picture of pulmonary disease mediated by *Rhodococcus equi* has been well described. Young foals aged 1–6 months are typically affected. Foals in this age category are particularly susceptible to infection because they are in an immunologic stage of waning maternal antibody. Most foals reach this age with its characteristic antibody 'trough' when warmer temperatures and dusty conditions are beginning to prevail, increasing the aerosolization of bacteria. Foals often present with an apparently acute onset of clinical disease characterized by

- fever
- tachypnea
- depression.

However the actual onset and early development of lesions in lung tissue is insidious and clinically silent. The disease process and degree of pulmonary involvement are typically well advanced by the time clinical signs are evident and a diagnosis is made. The incubation period may vary. In one study virulent organisms sprayed into the trachea of healthy foals resulted in the development of fever in 11–16 days. Evaluation of the thorax with radiography or ultrasound usually demonstrates the presence of cavitary lesions representing a multifocal, abscessing pattern of bronchopneumonia. The perihilar regions, and the cranial and cranioventral areas of the lungs tend to be most severely affected, and the hilar lymph nodes are often involved. In some cases a more atypical interstitial pneumonia may occur.

In addition to pulmonary disease, extrapulmonary manifestations of infection may be observed, including

- mesenteric lymphadenitis
- ulcerative colitis
- immune-mediated polysynovitis
- uveitis and keratoconjunctivitis
- osteomyelitis
- septic synovitis
- cutaneous pyogranulomas.

Of these extrapulmonary lesions, enteric disease (ulcerative colitis and mesenteric lymphadenitis) is the most common. Ulcerative colitis and/or mesenteric lymphadenitis were present concurrently with pneumonia in 50 per cent of foals with *Rhodococcus equi* infection in one survey. Any of the extrapulmonary manifestations of disease may precede signs of pneumonia, but once such clinical signs are observed, further evaluation will usually document the presence of underlying and concurrent pulmonary disease.

Intestinal colonization by *Rhodococcus equi* may include several manifestations. Enterocolitis in the form of diffuse infiltration of the lamina propria and submucosa by infected macrophages and multinucleate giant cells occurs. Affected segments have grossly thickened, corrugated mucosa with multiple, irregularly shaped, well-demarcated foci of necrosis and crateriform ulcers, from 0.5–4 cm in diameter. Histologically, the granulomatous infiltrate can be seen to fill the lamina propria, distort villi, and displace intestinal glands and crypts. These areas of granulomatous infiltrate are associated with those areas of the lamina propria and submucosa that are associated with lymphoid follicles. Cecal, colonic, and mesenteric lymph nodes may also become enlarged and firm. Foals with enteric infections commonly demonstrate the following clinical signs

- diarrhea
- fever
- variable weight loss.

In some cases cellular obstruction of the lymph nodes and lymphatic vessels leads to ascites; affected foals will show chronic weight loss and appear unthrifty and potbellied in addition to producing diarrhea. Although *R. equi* can be cultured from the stool of many foals or horses, documentation of increasing *R. equi* numbers in the feces, over the normal background numbers present, may be helpful in identifying clinically affected foals.

In the intestinal form of infection, it is likely that *Rhodococcus equi* utilizes the specialized microfold cells in the intestinal wall as a route of entry to macrophages in Peyer's patches and discrete lymphoid follicles diffusely distributed along the intestinal tract. These microfold cells, or M-cells, are interspersed among the villous enterocytes, and function as antigen-presenting cells, delivering lumenal antigen to immune cells in the submucosa and lamina propria for processing. Once the bacteria are ensconced within the phagosomes, they travel with the macrophage and may subsequently access lymph nodes in the mesentery of the small intestine, cecum, and large colon, causing enlargement and abscessation of these nodes. They may also enter the lacteal and lymph vessels, eventually gaining access to the circulation via the thoracic duct. The bacteria can then become hematogenously distributed, resulting in abscessation at random sites. Such abscesses often develop in the peritoneal cavity, but in horses and in other species, including humans, *R. equi* abscesses have been reported in a variety of locations. In humans, the organism has caused disease in both immunocompetent and immunocompromised individuals, though it occurs more commonly in patients with dysfunctional cell-mediated immunity such as HIV patients and transplant recipients. Respiratory tract disease, including chronic, granulomatous pneumonia and extrapulmonary infections such as mediastinitis, is the most common disease manifestation in humans, but thyroid abscesses, post-injection gluteal abscesses, renal abscesses, and a variety of other affected body sites have all been reported. Only about 30 per cent of humans with *R. equi* infections report any contact with herbivores or soil where herbivores have been.

TREATMENT AND PREVENTION

Diarrhea is the primary presenting sign in foals with abdominal lymphadenitis or colitis. Diarrhea may also develop as a complication of antimicrobial treatment with erythromycin and rifampin. The erythromycin/rifampin combination is the anti-rhodococcal treatment regimen of choice, because of

- the drugs' lipophilic properties, permitting good penetration across abscess walls and into the intracellular space of macrophages
- the synergistic action of the two agents combined.

Disruption of colon microflora is thought to cause the diarrhea in affected foals, necessitating (in some cases) adjustment of erythromycin doses to a lower rate in the recommended dose range or temporary discontinuation of the drugs for 24–48 hours. In some cases the diarrhea will be self-limiting and will not necessitate any alteration in dosing. Occasionally treatment with different antimicrobial drugs is necessary. Hyperthermia is another complication occasionally encountered in foals being administered erythromycin. The problem occurs most frequently in very hot weather when the thermoregulatory mechanisms are already challenged to a maximum in a pneumonic foal.

Successful management of farms with an enzootic *Rhodococcus equi* presence must address the issues of prophylactic measures for the disease, early identification of affected foals, and effective therapy of ill foals. Immune prophylaxis is an active area of research, and much remains to be elucidated and understood. For instance, administration of hyperimmune serum to young foals has been shown to reduce the incidence and mortality of *Rhodococcus equi* pneumonia on enzootic premises but is not effective at treating established disease. Vaccination of mares and their foals with a preparation of VapA protein extract was not protective for clinical disease and may have enhanced the likelihood of *R. equi* pneumonia in the foals. Preventative measures that are known to be effective, however, include

- prompt removal and composting of manure from infected foals
- rotating pastures to decrease erosion of pasture into dusty paddocks
- segregation of ill foals from the general population.

These measures effectively reduce the numbers of the infective organism in the environment, reducing the immune challenge to the at-risk population of foals in their immunologically vulnerable phase.

Equine cryptosporidial diarrhea

ND Cohen

INTRODUCTION

Diarrhea is a common and often serious disease of foals. Protozoal diarrhea in foals caused by the coccidian parasite *Cryptosporidium parvum* is being increasingly recognized. The purpose of this chapter is to review the epidemiology, clinical signs, diagnosis, treatment, and prevention of *C. parvum* infection in horses.

LIFE CYCLE AND TRANSMISSION

Infection of foals occurs by ingestion of the infective, sporulated oocysts. These excyst in the small intestine and attach to the epithelium in a location described as intracellular but extracytoplasmic. Amplification occurs both through asexual and sexual multiplication. Oocysts are formed that are capable of autoinfection prior to excretion (thin-walled oocysts) or that are immediately infectious when shed in feces (thick-walled oocysts). Transmission occurs either via the fecal–oral route or by ingestion of contaminated food or water. Sources of infection for horses are unknown but, as for people, contaminated municipal water may be important. Conflicting evidence exists as to whether mares are the source of infection for foals, however, in the author's experience mares are not the source of infection for foals. In Texas cattle do not appear to be an important source of infection for horses.

EPIDEMIOLOGY

Prevalence

Prevalence varies with the method of detection used and the population studied. Infection among clinically normal, mature horses is rare (approximately 0–5%). Prevalence at breeding farms may be higher, particularly among foals. Prevalence is higher among foals with diarrhea than among clinically normal foals, and prevalence may approach 100 per cent among diarrheic foals at farms during an outbreak.

Signalment

Foals are at increased risk of infection, particularly those from 1–4 weeks of age, however diarrhea associated with *Cryptosporidium parvum* may be seen in foals younger or older than this.

The time from infection to shedding oocysts for cryptosporidial diarrhea in foals is unknown. Most foals shedding cryptosporidial oocysts have been older than 5 days of age. Although cryptosporidial diarrhea has been described in foals with diarrhea observed at 2 days of age, cryptosporidial infection should be ranked lower in the differential diagnosis for diarrhea of a 2-day-old foal than in that of a foal aged 5–10 days. Cryptosporidial infection and diarrhea are rare in mature horses. Evidence of predisposition by sex or breed does not exist, although most epidemiological studies of equine cryptosporidiosis have been conducted in groups of mares and foals.

Immune status

Immunocompromised foals, such as those with severe combined immunodeficiency disease, are at increased risk. However, immunocompetent foals can also develop cryptosporidial diarrhea. Although the disease will generally be more severe among immunocompromised foals, severe or fatal diarrhea can occur in immunocompetent foals.

Farm epidemics

Some farms experience epidemics of cryptosporidial diarrhea. Recurrence during ensuing years is rare. A high density of foals, a municipal water source, foaling in stalls (versus pasture), and poor hygiene may be risk factors for infection and disease.

CLINICAL SIGNS

Clinical signs in foals vary with age and immune status and are usually limited to the gastrointestinal tract and related organs. Diarrhea associated with cryptosporidial infection is more prevalent during the first 3–4 weeks of life, but older foals, weanlings, and yearlings can be affected. Among immunocompromised foals with combined immunodeficiency, signs are often severe and can progress rapidly. In these foals sites other than the small intestine may be infected including the stomach, common bile duct, colon, and major pancreatic ducts. Among immunocompetent foals, clinical signs associated with cryptosporidial infection will vary from absent to fatal diarrhea. Inapparently infected foals may represent a source of infection for other foals. The severity of signs may be related to agent factors (inoculum size, virulence), host factors (age, immunocompetence), and environmental factors (water source, housing practices). In older foals (i.e. 3–6 months) the diarrhea may be more chronic and can persist until foals are 9–12 months of age. In all infected foals concurrent infection with other putative enteropathogens (*Salmonella* spp., rotavirus, coronavirus, adenovirus) may be observed.

DIAGNOSIS

Ante-mortem diagnosis of cryptosporidial infection is generally based on detection of oocysts in the feces. Fecal samples should be submitted as fresh material or in recommended preservative (10% formalin or sodium acetate-acetic acid-formalin). Oocysts can be detected using either concentration or staining techniques. Concentration of oocysts may be accomplished by flotation or sedimentation. Regardless of technique,

distinguishing oocysts from yeast is an important diagnostic issue.

In veterinary diagnostic laboratories, three techniques are commonly used

- flotation of oocysts
- acid-fast staining of oocysts
- detection of oocysts using an immunofluorescence assay (IFA).

Sedimentation techniques are rarely used in veterinary diagnostic laboratories. Of the flotation techniques used, flotation in Sheather's sugar solution is most common. Prompt processing is important because oocysts collapse and lose their spherical shape when left in Sheather's sugar solution.

Acid-fast staining of fecal specimens is widely used for detection of *Cryptosporidium parvum*. The technique is simple and staining kits are commercially available. The organisms appear as red spheres (4–6 mm in diameter) against a dark, counter-stained background, while yeast generally do not appear red (Plate 27.2). The technique has relatively poor specificity making it a poor choice for a screening test. However, it is useful clinically as a diagnostic test because of its good sensitivity, availability, and low cost.

The IFA test has relatively low sensitivity but excellent specificity. A commercial immunofluorescence assay is available (Meridian Diagnostics Inc., Cincinnati, OH) that simultaneously detects cryptosporidial and giardial organisms. The high cost relative to staining techniques and specialized microscopic equipment needed are limitations of the IFA. To date, reliable enzyme-linked immunosorbent assays have not been developed and validated for detecting *Cryptosporidium parvum* in samples from horses. Flow cytometric methods are more sensitive than IFA or acid-fast staining, but are not widely available.

The pattern of oocyst shedding by foals is variable in duration (from days to many weeks) and can be intermittent. Shedding may be antecedent, concurrent, or subsequent to the onset of diarrhea. Because of the variable duration and the intermittent pattern of shedding, multiple samples (at least three) should be submitted for detecting *Cryptosporidium parvum* in feces from foals. It may be easier to detect oocysts in unformed feces than in formed feces.

TREATMENT

Although over 120 different treatments have been tested in a variety of animals, to date no specific chemotherapy or immunotherapy has been proven to be convincingly effective for treating *Cryptosporidium parvum* in people and other mammals, and none has been evaluated in a controlled clinical trial among foals. Those treatments that may have greatest potential for use in foals include paromomycin and bovine colostrum.

Paromomycin is an expensive aminoglycoside antibiotic that is poorly absorbed from the gastrointestinal tract. Paromomycin reduced the duration and severity of diarrhea and eliminated oocyst shedding in neonatal calves experimentally infected with *Cryptosporidium parvum*. Paromomycin was effective in treating a cat with cryptosporidiosis. Doses used in calves have ranged from 50–100 mg/kg administered orally once or twice daily. No data exist for the use of this drug in foals. Adverse effects of paromomycin in humans include diarrhea, nausea, and abdominal cramps. As for all other agents used to treat cryptosporidial infection, experimental and clinical evidence also exists indicating a lack of effectiveness of paromomycin. No antibiotic approved for use in horses has been demonstrated to be effective in the treatment of cryptosporidial diarrhea.

Hyperimmune bovine colostrum has been used with varying success as a means of prophylaxis and therapy of cryptosporidiosis in animals and patients with AIDS. A factor limiting the use of hyperimmune bovine colostrum is its availability. Pooled bovine colostrum, however, is more readily available. Pooled bovine colostrum from non-immunized animals also may be protective in controlling cryptosporidiosis; non-immunoglobulin factors in the colostrum may provide protection. Use of hyperimmune or pooled bovine colostrum has not been uniformly successful. The benefits of administration of colostrum or hyperimmune colostrum to foals, regardless of their age, with cryptosporidiosis is unknown.

Treatment of foals with severe combined immunodeficiency is likely to be unsuccessful. In immunocompetent foals, infection is often subclinical or mild and self-limiting; in these foals no treatment or supportive care is needed. In more severely affected foals further treatment may be necessary.

CONTROL AND PREVENTION

The prevention and control of cryptosporidiosis can be difficult. Currently, immunization effective at preventing cryptosporidiosis in horses and foals is lacking. Although some chemotherapeutic agents have shown preventive potential, the cost-effectiveness of such prophylaxis is often a limiting factor. Oocysts shed in feces are infective, extremely resistant to environmental factors, and can survive for months if not exposed to

extremes of temperature or desiccation. Oocysts can be killed by steam, 10% formalin, 5% ammonia, and undiluted commercial bleach, although prolonged exposure is necessary which can be difficult to achieve. Good sanitation may help by decreasing the oocyst burden in the foals' environment. Specific sanitation strategies would include providing uncontaminated water, rigorous cleaning (preferably with steam) and disinfecting foaling stalls, removing all the bedding, and isolating diarrheic foals.

ZOONOTIC CONSIDERATIONS

Ingestion of oocysts in people can cause gastrointestinal disease in immunocompetent and immunosuppressed people. People working with animals, including farmers and veterinarians, are considered to be at increased risk. Cryptosporidiosis has occurred in veterinary students exposed to infected calves and foals. Efforts to minimize transmission in persons handling infected foals should include instruction regarding, and rigorous attention to, hygiene, protective clothing (possibly to include face mask, gloves, gown or coveralls, and boots), and efforts to disinfect contaminated areas. Persons with primary or acquired immunodeficiency should not be exposed to foals with diarrhea in which a diagnosis of cryptosporidiosis is possible. Because of the low prevalence of infection, mature horses do not appear to be an important source of environmental contamination.

Diarrhea – other causes

JF Freestone

ANTIBIOTIC-INDUCED DIARRHEA

Antibiotic-induced diarrhea occurs because of the inhibition of the normal anaerobic bacterial flora and the secondary proliferation of pathological bacteria. In adult horses antibiotic-induced colitis is generally severe and can rapidly be fatal. In foals antibiotic-induced diarrhea is generally mild and will often resolve quickly once the antibiotics are discontinued.

Diarrhea can be induced by a number of antibiotics. Some antibiotics will cause a problem only in certain regions and this is probably a reflection of differences in the normal intestinal bacterial flora. In foals the antibiotic most commonly associated with diarrhea is erythromycin. Erythromycin is widely used in combination with rifampin for the treatment of *Rhodococcus equi* infections. Diarrhea that develops in a foal on erythromycin will generally resolve 48 hours after the antibiotic is discontinued. Often the foal needs to continue receiving antibiotics for the *R. equi* infection. Trimethoprim sulfamethoxazole and rifampin can be used when problems of either hyperthermia or diarrhea have developed secondary to the use of erythromycin. *R. equi* infections have resolved in response to this antibiotic combination.

SEPTICEMIA

Diarrhea is a common clinical sign in the septicemic foal. Septicemia usually develops in the first 7 days of life. Foals may be normal at birth, become infected and then deteriorate, or be born septicemic with weakness and inability to stand and nurse. The common clinical signs in the septicemic foal initially are lethargy, depression, and failure to nurse, followed by diarrhea. The common bacteria implicated in neonatal septicemia are *Escherichia coli, Actinobacillus* spp., *Klebsiella pneumoniae,* and *Streptococcus* spp. The basis for treatment of these foals is antibiotics to kill the infectious agent with supporting medical therapy and nursing care for the neonate.

Another foal diarrhea syndrome which has not been widely reported has been termed 'fetal diarrhea'. The newborn foal with fetal diarrhea will be born covered in liquid yellow-brown feces. These foals are infected *in utero,* and there may be an accompanying placentitis. The amniotic fluid is contaminated with feces and the foal is subject to aspiration pneumonia. These foals are generally septicemic and may appear healthy and robust at birth but will often be unable to stand and will then rapidly deteriorate. Other foals born with fetal diarrhea will progress normally and it is assumed these foals develop diarrhea shortly prior to birth and have limited exposure to the severely contaminated environment. All foals born with evidence of fetal diarrhea should be treated with broad spectrum antibiotics and closely monitored for signs of deterioration.

NUTRITIONAL CAUSES OF DIARRHEA

Nutritional causes of diarrhea in foals have been associated with overfeeding, use of milk replacers, and a rapid change in diet from mare's milk to milk replacers (e.g. orphaned foals). In foals deprived of mares colostrum and milk for 48 hours because of the possibility of neonatal isoerythrolysis, and supplemented with milk replacer, it is common for a self-limiting diarrhea to

develop. Foals with these forms of diarrhea remain clinically normal.

Lactase deficiency and lactose intolerance have both been reported in foals. These are both are unusual causes of diarrhea. Lactase deficiency can be evaluated by use of an oral lactose tolerance test.

Ingestion of sand and dirt by foals can also cause diarrhea secondary to local irritation of the lining of the gastrointestinal tract. Diagnosis can be made by examining the feces for sand or in severe cases using abdominal radiography. Treatment with orally administered methyl cellulose may be effective in removing the sand and dirt.

EQUINE HERPESVIRUS

Foals infected *in utero* with equine herpesvirus may develop diarrhea although it is not the predominant clinical sign in these foals. Often the infected foal will appear normal at birth but will fail to stand and nurse and then progressively deteriorate, developing severe respiratory distress terminally. These foals are treated and supported as septicemic foals, although treatment is generally unsuccessful. A definitive diagnosis is made on histopathological changes in the lung, liver, and the lymphoreticular tissues at necropsy.

CANDIDIASIS

Candida albicans is a commensal organism of the mucous membranes and gastrointestinal tract. Superficial infections have been reported in foals. Systemic candidiasis is rare and generally occurs in foals treated with prolonged broad spectrum antibiotics for septicemia. Immunocompromised foals are also predisposed to candidiasis.

Diarrhea has been reported in foals with systemic candidiasis, but this is considered an unusual cause. As these foals are often immunocompromised or have been treated long term with antibiotics, the diarrhea may not be directly due to the Candida infection.

PARASITES

Strongyloides westeri

Strongyloides westeri is a questionable cause of diarrhea in young foals. Transmission occurs by ingestion of infective larvae from the mare's milk or via skin penetration. The pre-patent period is 8–14 days. Attempts to establish a clear association between infective larvae and the induction of diarrhea have been unsuccessful. Treatment of mares on the day of parturition with ivermectin was unsuccessful in blocking vertical transmission. Treating foals with ivermectin or oxibendazole is effective.

Strongyle infections

Equine strongylosis occurs secondary to mixed infections with large strongyles and cyathostomes (small strongyles). These mixed infections cause gastrointestinal tract irritation and clinical signs of intermittent soft feces, but can also cause persistent diarrhea in foals. The severity of the clinical signs is related to the parasite load. Foals grazing pasture containing high levels of strongyle eggs, or immunologically naïve foals with a good worming history that are subsequently exposed to strongyle infections are at risk of developing clinical signs of strongyle parasitism. These clinical signs include lethargy, depression, decreased weight gain, a rough hair coat, and diarrhea. Treatment with ivermectin is effective in controlling these mixed infections.

Proliferative enteropathy in foals

J-P Lavoie and R Drolet

Proliferative enteropathy is a transmissible enteric disease affecting a number of mammalian species, notably pigs. It has a worldwide distribution and its causal agent has been recently identified and classified as *Lawsonia intracellularis*, an obligate intracellular bacterium.

CLINICAL PRESENTATION

The disease has been described sporadically in horses, either as isolated cases or as outbreaks in breeding farms. Foals 4–7 months of age appear most susceptible to the disease. Common clinical signs include depression, rapid and severe weight loss, subcutaneous edema, diarrhea, and colic. Extremely poor body condition with a rough hair-coat and a pot-bellied appearance are common findings in affected foals. The disease may lead to death within a few days or cause chronic growth retardation. Concomitant respiratory tract infection and intestinal parasitism are also found in some foals.

CLINICAL PATHOLOGY

Hypoproteinemia is the most consistent laboratory finding. Other commonly observed abnormalities include transient leukocytosis, anemia, increased creatine kinase, hypocalcemia, hypochloremia, and hyponatremia.

DIFFERENTIAL DIAGNOSIS

The clinical signs presented by foals with proliferative enteropathy resemble those associated with common gastrointestinal diseases caused by parasites, infections caused by *Salmonella* spp., *Clostridium* spp., and *Rhodococcus equi*, or sand impactions. However, these conditions are unlikely to cause outbreaks of disease characterized by weight loss, diarrhea, colic, and severe hypoproteinemia in foals of this age group.

DIAGNOSIS

Post-mortem diagnosis of proliferative enteropathy is based on identifying the characteristic intracellular bacteria within the apical cytoplasm of proliferating crypt epithelial cells of the intestinal mucosa, using a silver stain (Figure 27.2). The severe hyperplasia of the intestinal crypts often causes a grossly detectable thickening of the mucosa of the distal small intestine. Polymerase chain reaction analysis and immunohistochemistry confirm the presence of *Lawsonia intracellularis* in intestinal tissue. Isolation of the organism is not a practical means of diagnosis as it cannot yet be cultivated in conventional cell-free media and the technique is available in only a few research institutions.

Ante-mortem diagnosis of proliferative enteropathy is based on clinical signs, hypoproteinemia, and the exclusion of common enteric infections. The presence of the organisms can be detected using polymerase chain reaction analysis of fecal samples. Although specific, to date this technique has revealed a low sensitivity in horses. The use of serology for the diagnosis of *Lawsonia intracellularis* infection in a small number of foals suggests that this technique may be promising.

THERAPY

Erythromycin estolate (25 mg/kg p.o. q. 6–8 h) alone or combined with rifampin (7 mg/kg p.o. q. 12 h) for a minimum of 21 days is effective in controlling the disease. Additional symptomatic treatment such as antimicrobial, anti-ulcer therapy and parenteral feeding may be required in some foals. Foals with severe hypoproteinemia may benefit from administration of plasma intravenously.

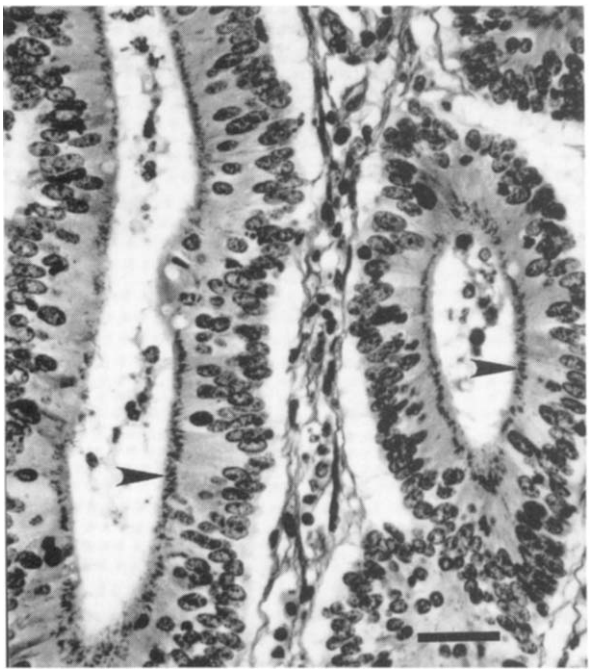

Figure 27.2 Intestinal crypts from a foal with proliferative enteropathy. Numerous bacteria are agglomerated within the apical cytoplasm of the crypt enterocytes (arrow heads). Warthin Starry silver stain.

OUTCOME

Without appropriate antimicrobial therapy the disease may lead to death. However a rapid improvement (<24–48 h) in attitude, appetite, weight gain, and colic signs or diarrhea may be observed in foals following administration of erythromycin and/or rifampin. The increase in plasma protein concentration lags compared to the improvement noted on other parameters during therapy.

BIBLIOGRAPHY

Foal heat diarrhea

Becht J L, Semrad S D (1986) Gastrointestinal diseases of foals. *Comp. Cont. Educ. Pract. Vet.* 8(7):S367–S374.

Masri M D, Merritt A M, Gronwall R, Burrows C F (1986) Fecal composition in foal heat diarrhea. *Equine Vet. J.* 18(4):301–6.

Viral diarrhea

Cohen N (1997) Diarrheal diseases of foals. In: *Current Therapy in Equine Medicine* 4th edn, N Robinson (ed.), W B Saunders, Philadelphia, p. 631.
Fenger C (1998) Neonatal and perinatal diseases. In: *Equine Internal Medicine*, S Reed and W Bayly (eds). W B Saunders, Philadelphia, pp. 962–3.
Smith B (1996) Diarrhea. In: *Large Animal Internal Medicine* 2nd edn, B P Smith (ed.). C V Mosby, St Louis, pp. 119–123.

Salmonellosis in the foal

Clarke R C, Gyles C L (1993) Salmonella. In: *Pathogenesis of Bacterial Infections in Animals*, 2nd edn, C L Gyles and C O Thoen (eds). Iowa State University Press, Ames, IA, pp. 133–53.
Jones S L, Spier S J (1998) Inflammatory diseases of the large intestine causing diarrhea. In: *Equine Internal Medicine*. S M Reed and W M Bayly (eds). Philadelphia, W B Saunders, Philadelphia, pp. 663–7.
Kowalski J J. Bacterial and mycotic infections. In: *Equine Internal Medicine*. S M Reed and W M Bayly (eds). Philadelphia, W B Saunders, Philadelphia, pp. 68–70.
Madigan J E(1991) Neonatal salmonellosis. In: *Manual of Equine Neonatal Medicine*, 2nd edn, J E Madigan (ed.). Live Oak Publishing, Woodland, CA; pp. 133–5.
Madigan J E (1995) Diarrhea in neonatal foals. In: *Large Animal Internal Medicine*, 2nd edn, B P Smith (ed.). Mosby Year Book, St Louis, MO; pp. 391–4.
Spier S J (1993) Salmonellosis. *Vet. Clin. N. Am. Equine Pract.*; 9:2 385–7.
Vaala W E (1996) Failure of passive-transfer: diagnosis, treatment and prevention. In: *Proceedings of Equine Stud Medicine*. Post Graduate Foundation of Veterinary Science, University of Sydney, Sydney, Australia; pp. 31–8.
Vaala W E (1996) Neonatal foal diarrhea. In: *Proceedings of Equine Stud Medicine*. Post Graduate Foundation of Veterinary Science, University of Sydney, Sydney, Australia; pp. 133–5.
Vaala W E (1996) Neonatal septicemia. In: *Proceedings of Equine Stud Medicine*. Post Graduate Foundation of Veterinary Science. University of Sydney, Sydney, Australia; pp. 211–18.

Clostridial enterocolitis in foals

East L M, Savage C J, Traub-Dargatz J L *et al.* (1998) Enterocolitis associated with *Clostridium perfringens* infection in neonatal foals: 54 cases (1988–1997). *J. Am. Vet. Med. Assoc.* 212(11):1751–6.
Meer R R, Songer J G (1997) Multiplex polymerase chain reaction assay for genotyping *Clostridium perfringens*. *Am. J. Vet. Res.* 58(7):702–5.
Netherwood T, Binns M, Townsend H *et al.* (1998) The *Clostridium perfringens* enterotoxin from equine isolates; its characterization, sequence and role in foal diarrhea. *Epidemiol. Infect.* 120:193–200.

Rhodococcus equi as an agent of intestinal disease

Anzai T *et al.* (1997) Comparison of tracheal aspiration with other tests for diagnosis of *Rhodococcus equi* pneumonia in foals. *Vet. Microbiol.* 56(3–4): 335–45.
Barton M D, Hughes K L (1984) Ecology of *Rhodococcus equi*. *Vet. Microbiol.*; 9:65–76.
Brumbaugh G W, Davis L E, Thurman J C, *et al.* (1990) Influence of *Rhodococcus equi* on the respiratory burst of resident alveolar macrophages from adult horses. *Am. J. Vet. Res.*; 51:766–71.
Giguere S, Prescott J F (1997) Strategies for the control of *Rhodococcus equi* infections on enzootic farms. *Proc. Am. Assoc. Equine Pract.*; (43):65–70.
Hondalus M K (1997) *Rhodococcus equi*: Pathogenesis and virulence. *Proc. Am. Assoc. Equine Pract.*; 43:71–8.
Prescott J F, Hoffman A M (1993) *Rhodococcus equi*, *Vet. Clin. N. Am. Equine Pract.*; 9(2):375–84.
Prescott J F *et al.* (1996) Use of a virulence-associated protein based ELISA for *Rhodococcus equi* serology in horses. *Equine Vet. J.* 28(5):344–9.
Takai S *et al.* (1986) Quantitative fecal culture for early diagnosis of *Corynebacterium (Rhodococcus) equi* enteritis in foals. *Can. J. Vet. Res.*; 50(4):479–84.
Tizard I (1996) Immunity at body surfaces. In: *Veterinary Immunology* 5th edn, I R Tizard (ed.). W B Saunders, Philadelphia, pp. 254–55.
Zink M C, Yager J A, Smart N L (1986) *Corynebacterium equi* infections in horses, 1958–1984: a review of 131 cases. *Can. J. Vet. Res.* 27:213.
Zink M C, Yager J A, Prescott J F *et al.* (1987) Electron microscopic investigation of intracellular events after ingestion of *Rhodococcus equi* by foal alveolar macrophages. *Vet. Microbiol.*; 14:295–305.

Equine cryptosporidial diarrhea

Cohen N D, Snowden K (1996) Cryptosporidial diarrhea in foals. *Comp. Cont. Educ. Pract. Vet.* 18:298–306.
Cole D J, Cohen N D, Snowden K, Smith R (1998) Prevalence and risk factors for fecal shedding of *Cryptosporidium parvum* oocysts in horses. *J. Am. Vet. Med. Assoc.* 213:1296–1302.
Cole D J, Snowden K, Cohen N D, Smith R (1999) Detection of *Cryptosporidium parvum* in horses: thresholds of acid-fast stain, immunofluorescence assay, and flow cytometry. *J. Clin. Microbiol.* 37.
Xiao L, Herd R P (1994) Review of equine Cryptosporidium infection. *Equine Vet. J.* 26:9–13.

Diarrhea – other causes

Becht J L, Semrad S D (1986) Gastrointestinal diseases of foals. *Comp. Cont. Educ. Pract. Vet.* 8:S367–S374.
Klei T R (1986) Other parasites – recent advances. *Vet. Clin. N. Am. Equine Pract.* 2: 329–36.
Martens R J, Malone P S, Brust D M (1985) Oral lactose tolerance test in foals: techniques and normal values. *Am. J. Vet. Res.* 46: 2163–6.
McClure J J, Addison J D, Miller R I (1985) Immunodeficiency manifested by oral candidiasis and bacterial septicemia in foals. *J. Am. Vet. Med. Assoc.* 186:1195–7.
Reilly L K, Palmer J E (1994) Systemic candidiasis in four foals. *J. Am. Vet. Med. Assoc.* 205:464–6.
Thamsborg S M, Leifsson P S, Grondahl C, Larsen M, Nansen P (1998) Impact of mixed strongyle infections in foals after one month on pasture. *Equine Vet. J.* 30:240–5.

Proliferative enteropathy in foals

Duhamel G E, Wheeldon E B (1982) Intestinal adenomatosis in a foal. *Vet. Pathol.*; 19:447–9.

Frank N, Fishman C E, Gebhart C J *et al.* (1998) *Lawsonia intracellularis* proliferative enteropathy in a weanling foal. *Equine Vet. J.*; 30:549–52.

Lavoie J P, Parsons D, Drolet R (1998) Proliferative enteropathy in foals: a cause of colic, diarrhea and protein-losing enteropathy. *Proc. Am. Assoc. Equine Pract.* 44:134–5.

McOrist S, Gebhart C J, Boid R *et al.* (1995) Characterization of *Lawsonia intracellularis* gen. nov., sp. nov., the obligately intracellular bacterium of porcine proliferative enteropathy. *Int. J. Syst. Bacteriol*; 45:820–5.

Williams N M, Harrison L R, Gebhart C J (1996) Proliferative enteropathy in a foal caused by *Lawsonia intracellularis*-like bacterium. *J. Vet. Diag. Invest*; 8:254–6.