Acute colitis is well recognized in horses and ponies and can be fatal even if aggressive therapy is administered. This article addresses the common infectious causes of acute colitis (TABLE 1). Acute colitis most often affects individual horses, but associated infectious agents may cause disease outbreaks (e.g., salmonellosis, intestinal clostridiosis) and may carry a zoonotic risk. Prompt recognition of acute colitis by the attending clinician and an appropriate isolation protocol are critical for limiting the risk to unaffected horses and humans. As with many diseases, the fecal–oral route is the main way in which horses or humans contract infectious enteric diseases.

Unlike many noninfectious etiologies for which diagnostic testing is limited, tests such as whole blood polymerase chain reaction (PCR) testing and tests for fecal samples (e.g., bacterial culture, PCR testing, toxin ELISAs) are available to detect common infectious causes of acute colitis. However, while these tests may help determine a definitive diagnosis, results are often not obtained in a timely manner, and treatment should not be delayed pending results.

Salmonella spp

Salmonellosis is the most frequently diagnosed infectious cause of diarrhea in horses. Salmonella spp are gram-negative facultatively anaerobic bacteria. Numerous serotypes can infect horses, with those in groups B (including Salmonella ser Typhimurium and Salmonella ser Agona) and C2 (Salmonella newport) appearing to be associated with disease more often than those in other groups. Four clinical syndromes of Salmonella infection are commonly described and have been reproduced experimentally in horses:

At a Glance

- **Salmonella spp**
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Abstract: Infectious causes of acute colitis are of considerable concern to horse owners. Acute infectious colitis not only is a severe, potentially fatal disease but also carries a risk of disease outbreak in a group of horses. Understanding commonly recognized infectious etiologies can help clinicians address each case appropriately, limit the risk of disease spread, and optimize the patient's chance of survival. This article highlights the key points regarding infectious etiologies of acute colitis in adult horses (i.e., older than 12 months).
**TABLE 1 Infectious Causes of Acute Colitis in Horses**

<table>
<thead>
<tr>
<th>Differential</th>
<th>Etiologic Factor Involved</th>
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<tbody>
<tr>
<td>Salmonellosis</td>
<td>Large number of <em>Salmonella</em> serotypes</td>
</tr>
<tr>
<td>Intestinal clostridiosis</td>
<td><em>Clostridium difficile</em></td>
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<tr>
<td></td>
<td><em>Clostridium perfringens</em></td>
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<tr>
<td>Potomac horse fever</td>
<td><em>Neorickettsia risticii</em></td>
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</tbody>
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- Inapparent infections; latent or active carrier states
- Acute diarrhea
- Depression, fever, anorexia, and neutropenia without diarrhea or colic
- Septicemia with or without diarrhea

In acute cases of *Salmonella* enterocolitis, the first step in the pathogenesis involves disruption of the host’s defenses, including gastric pH, gastrointestinal (GI) motility, colonization resistance, and mucosal immunity. This permits colonization of the distal small intestine and the colon by *Salmonella* bacteria attaching to and entering mucosal epithelial cells in the ileum, cecum, and proximal large colon. The common portal of entry into intestinal cells is the brush border, but bacteria can also penetrate via tight junctions. Bacteria enter the lamina propria, are phagocytosed by mucosa-associated macrophages, and then multiply intracellularly and initiate local inflammation. Leukocytes are recruited and activated, resulting in production of prostaglandins, leukotrienes, reactive oxygen metabolites, and histamine. Damaged mucosal epithelial cells and activated macrophages produce proinflammatory cytokines (e.g., interleukin-1, tumor necrosis factor α), which further up-regulate the local inflammatory response. When these cytokines reach the circulation, they initiate a systemic inflammatory response (e.g., fever, tachycardia, tachypnea). While *Salmonella* organisms that have crossed the mucosal barrier may enter the bloodstream (either directly or via the lymphatic system), in most cases, bacteria do not disseminate beyond intestinal mucosa and mesenteric lymph nodes.

Additional pathogenic mechanisms demonstrated by *Salmonella* bacteria include toxin production and increased colonic secretion. *Salmonella*-associated cytoxin inhibits protein synthesis in mucosal cells, causing morphologic damage and altered permeability. Virulent salmonellae also produce enterotoxin similar to the heat-labile toxin produced by *Escherichia coli*. This enterotoxin increases secretion of chloride and water by colonic mucosal cells via a prostaglandin-mediated increase in intracellular cAMP. Due to severe tissue injury and the ensuing inflammatory response, acute enterocolitis caused by *Salmonella* organisms is characterized by severe fibrinonecrotic typhlocolitis with interstitial edema and variable degrees of intramural vascular thrombosis that may progress to infarction. Recovery of normal large intestinal function typically takes at least 5 to 7 days, but mucosal injury may be severe enough that normal function will not return and diarrhea will become chronic.

**Clostridium difficile**

*Clostridium difficile* is an obligate anaerobic, spore-forming, gram-positive rod that is environmentally ubiquitous in spore form. It was first identified in human neonatal feces in 1935. *C. difficile* organisms are among the first bacteria acquired after a foal’s birth, representing a component of the normal GI flora of foals and adult horses. *C. difficile* has been reported to cause acute enterocolitis in humans and horses and is now recognized as the primary cause of nosocomial and antimicrobial-associated diarrhea and colitis in humans. While salmonellosis is reportedly the most common infectious cause of acute colitis in horses, the incidence of *C. difficile*-associated colitis appears to be increasing. The involvement of *C. difficile* in equine enteric disease was first established in 1987, when the organism was associated with diarrhea in 27 of 43 foals in an enterocolitis outbreak. Disruption of GI flora by stress, antimicrobial therapy, or other factors allows overgrowth of *C. difficile*; subsequent release of toxins leads to acute diarrhea.

*C. difficile* is considered the most common enteric pathogen in hospitalized humans. *C. difficile* infection is usually associated with antimicrobial therapy; in humans, the risk of contracting the disease increases as antimicrobial treatment continues. Additional risk factors for *C. difficile* infection in horses include severe underlying disease, presence of a nasogastric tube, dietary change, starvation, transportation, and administration of antiulcer medication.

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**CriticalPoint**

Understanding infectious causes of acute colitis is important for preventing disease spread in the equine population.
Hospitalization and antimicrobial therapy are also risk factors for development of C. difficile colitis in horses; in one study, 18 of 43 (42%) horses that developed acute colitis during antimicrobial treatment cultured positive for C. difficile. In horses, a wide variety of antimicrobials have been associated with C. difficile diarrhea; however, orally administered antimicrobials, or antimicrobials recycled via the enterohepatic system, have been shown to be most likely to increase the number of clostridial colony-forming units in equine feces.

A horse can be infected by vegetative cells or spores of C. difficile from other infected horses, a contaminated environment, or humans. C. difficile spores are not easily destroyed in the environment; they can survive in inoculated feces for at least 4 years. Another possible route of infection is proliferation of C. difficile spores in the GI tracts of subclinical carriers. If normal GI flora is disrupted (e.g., by a dietary change, antimicrobial administration, or GI surgery), the risk of establishment and proliferation of C. difficile increases. Following ingestion, C. difficile spores survive the low pH of the stomach and upper small intestine, germinate in the terminal ileum, and multiply in the colonic lumen. In the absence of competition from indigenous microflora, the number of bacteria increases, producing toxins that damage intestinal tissue.

Assessment of C. difficile involvement is further complicated because not all strains of C. difficile can cause disease. Pathogenic strains produce at least five different toxins, of which toxins A and B have been studied in most detail. Adenosine diphosphate–ribosyltransferase (binary toxin) was recognized recently, but its role in disease has not been determined. Toxin A, an enterotoxin, is thought to have the most significant role regarding induction of fluid secretion, inflammation, and characteristic alterations in intestinal morphology. Toxin A also weakens the tight junctions between epithelial cells lining the colon, helping toxin B enter epithelial cells. Toxin A induces neutrophil influx into intestinal tissue as well as mast cell degranulation and secretion of prostaglandins, histamine, inflammatory cytokines, and 5-hydroxytryptamine by activated leukocytes, leading to vasodilatory and secretory responses in enterocytes. Toxin B has profound cytotoxic effects in vitro and is more than 1000 times more cytotoxic than toxin A but has demonstrated minimal damage to intact intestinal mucosa. However, a toxin A–negative, toxin B–positive strain of C. difficile has been implicated in human colitis, suggesting that toxin B may also be pathogenic.

**Clostridium perfringens**

Clostridium perfringens is similar to C. difficile in its appearance, physiologic requirements, and environmental behavior. It is considered a normal inhabitant of the GI tract of horses, with positive identification on fecal culture in 12% to 22% of healthy adult horses and 90% of 3-day-old foals. Diet factors such as antimicrobial treatment and stressful stimuli can induce intestinal dysbiosis characterized by an overgrowth of C. perfringens. However, unlike C. difficile, which has been recognized as a cause of colitis in horses with no predisposing factors, there is debate as to whether C. perfringens can be a primary cause of colitis in adult horses. Experimental administration of C. perfringens enterotoxin to ponies has been documented to cause clinical signs of colitis, suggesting that this bacterium can be pathogenic in adult horses. Certainly, if C. perfringens overgrowth occurs, large quantities of enterotoxin could be produced, possibly having pathogenic effects on the colon and leading to clinical signs of colitis.

The many genetically distinct strains of C. perfringens have variable virulence and produce one or more exotoxins. The pattern of exotoxin production is used to classify C. perfringens into five biotypes: A, B, C, D, and E. C. perfringens type A is the most common clostridial isolate from healthy horses of all ages but is also the most common isolate from adults and foals with diarrhea; therefore, the organism may cause disease if overgrowth occurs. Type C is the most commonly reported clostridial enteric pathogen in foals in North America. The identification of C. perfringens types B, D, or E from clinical cases of colitis is rare.

All five C. perfringens biotypes produce α-toxin, which hydrolyzes lecithin complexes in the membranes of capillary endothelium and other cells as well as in mitochondria. This results in impaired glucose uptake and energy production as well as in activation of arachi-
Acute Colitis: Infectious Causes

Potomac Horse Fever

Potomac horse fever (equine monocytic ehrlichiosis) is caused by the obligate intracellular rickettsial organism Neorickettsia risticii. This organism’s role in Potomac horse fever was established more than 20 years ago when inoculation of a horse with blood from an infected horse led to development of clinical signs. However, until reliable PCR tests were developed and recent studies completed, the life cycle remained undefined. Studies have now shown that the causative rickettsial organisms live within trematodes. These trematodes are ingested by freshwater operculate snails and aquatic insects that become intermediate hosts. Bats and birds may be definitive hosts of the helminth vector and a natural reservoir of N. risticii, but the definitive host of N. risticii remains a subject of debate. However, the mechanism of transmission of N. risticii to horses has been clarified by challenge studies. Ingestion of numerous intermediate hosts, namely aquatic insects, including stoneflies, mayflies, and aquatic water snails, leads to development of clinical signs consistent with Potomac horse fever, whereas percutaneous inoculation with N. risticii did not result in clinical disease.

In horses, N. risticii targets the GI mucosa. The resulting lesions are most severe in the large intestine. The organisms locate within mucosal epithelium as well as macrophages and mast cells of the lamina propria. They survive within macrophages by inhibiting production of reactive oxygen species and blocking phagosome–lysosome fusion, thereby avoiding lysosomal digestion. Intracellular cAMP increases within infected host cells, leading to decreased luminal reabsorption of sodium ions, increased chloride ion secretion, and decreased water reabsorption in the colon, resulting in profuse watery diarrhea. In addition, when infected cells fill with rickettsial organisms, cell lysis occurs. As the disease progresses, fibrinous necrotizing typhlocolitis with severe mucosal ulceration and inflammation of the lamina propria may occur. Vasculitis and intravascular coagulation with perivascular edema in the large intestine are consistent pathologic features of N. risticii infection.

While the infectious organism has been identified in aquatic snails from many areas of the world, Potomac horse fever is clinically recognized only in North America, South America, and Europe. The disease is most common from late summer through early fall, with a peak incidence in July and August in the northern hemisphere. Potomac horse fever is characterized by fever, anorexia, depression, diarrhea, and leukopenia. When Potomac horse fever is experimentally induced by oral inoculation, the latent period is typically 1 to 3 weeks, with a biphasic pattern of fever preceding development of diarrhea. While initial fever may be as high as 107°F (41.7°C), it is often undetected in horses in the field, and there is no indication of infection until onset of the second episode of fever in conjunction with severe depression and diarrhea. Moderate to severe diarrhea is known to occur in 75% of horses with Potomac horse fever and may persist for several days. While laminitis is a complicating factor known to develop in 20% to 30% of Potomac horse fever cases, the pathogenesis of this condition remains unclear.

Other complications of Potomac horse fever may include abortion of infected fetuses, vascular thrombosis, renal failure, and protein-losing enteropathy.

Conclusion

Infectious causes of acute colitis have a common clinical presentation despite variation in...
associated underlying pathophysiology. Because of the time delay associated with many diagnostic tests, the risk of disease transmission is considerable. Prompt patient isolation and owner education are essential to limiting the chance of disease outbreak. Awareness of the infectious causes of acute colitis should prompt diagnostic testing. If a definitive diagnosis is reached, appropriate treatment can be employed, and the chance for a favorable outcome increases.

References

Acute Colitis: Infectious Causes

This article qualifies for 3 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. Subscribers may take individual CE tests online and get real-time scores at CompendiumEquine.com. Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program.

1. Which of the following is the most commonly reported infectious cause of colitis in horses?
   a. Salmonella spp
   b. C. difficile
   c. C. perfringens
   d. N. risticii
   e. none of the above

2. Which statement is not applicable to the pathophysiology of Salmonella enterocolitis?
   a. Salmonella bacteria are intracellular organisms.
   b. Systemic salmonellosis is possible by penetration of the bacterium into the bloodstream and the lymphatic system.
   c. The bacteria trigger an inflammatory response in the cells of the large intestine.
   d. Some Salmonella spp produce enterotoxin.
   e. Salmonella spp avoid lysosomal digestion by blocking phagosomal–lysosome fusion.

3. Which statement regarding Salmonella spp is true?
   a. Salmonella spp are gram positive.
   b. Salmonella spp are obligate anaerobes.
   c. The virulence of Salmonella bacteria varies tremendously with serotype.
   d. Salmonella bacteria do not produce toxins.
   e. S. Typhimurium is rarely associated with disease.

4. Which of the following is not a risk factor for C. difficile-associated colitis in horses?
   a. presence of a nasogastric tube
   b. hospitalization
   c. antimicrobial administration
   d. laminitis
   e. dietary change

5. Which statement regarding C. difficile is incorrect?
   a. C. difficile spores can survive for long periods of time in the environment.
   b. Toxin A is an enterotoxin.
   c. Different strains of C. difficile produce different types of toxin.
   d. Toxin A is 1000 times more cytotoxic than toxin B.
   e. Binary toxin was recognized recently and may have pathogenic significance.

6. Which statement regarding C. perfringens is incorrect?
   a. C. perfringens type B is a common cause of equine acute colitis.
   b. α-Toxin is produced by all five types of C. perfringens.
   c. C. perfringens is a normal inhabitant of the equine GI tract.
   d. C. perfringens type A can produce enterotoxin.
   e. C. perfringens can cause colitis due to bacterial overgrowth, which often occurs secondary to a trigger such as antimicrobial administration.

7. Which statement regarding intestinal clostridiosis in horses is incorrect?
   a. The incidence of equine intestinal clostridiosis is decreasing in North America.
   b. Intestinal clostridiosis is highly contagious.
   c. Clostridial spores are difficult to destroy in the environment.
   d. Antimicrobial therapy is a risk factor for development of intestinal clostridiosis.
   e. Adult horses can develop clostridial-associated acute colitis.

8. Which statement regarding Potomac horse fever is incorrect?
   a. The disease is common in late summer through early fall.
   b. Laminitis can occur in 20% to 30% of cases.
   c. N. risticii is transmitted by ticks.
   d. Not all horses with the disease develop diarrhea.
   e. Characteristic signs of the disease include fever, depression, anorexia, and leukopenia.

9. Which statement regarding Potomac horse fever is true?
   a. The disease is recognized worldwide.
   b. Percutaneous inoculation of N. risticii can result in clinical disease.
   c. Aquatic water snails are the definitive host for N. risticii.
   d. The latent period is 1 to 2 days when Potomac horse fever is experimentally induced.
   e. Complications of the disease include laminitis, abortion, vascular thrombosis, renal failure, and protein-losing enteropathy.

10. Which statement regarding infectious causes of acute colitis in adult horses is incorrect?
    a. Due to diagnostic limitations for acute colitis, precautionary measures, including patient isolation, should be employed for every case of acute diarrhea.
    b. The fecal–oral route is the most common way in which the disease is transmitted.
    c. Many infectious causes of acute colitis are potentially zoonotic.
    d. There are limited diagnostic tests available for fecal samples in acute colitis cases.
    e. Laminitis and endotoxemia are potentially fatal sequelae in cases of acute colitis.