

THERAPEUTIC MANAGEMENT OF GASTROINTESTINAL DISORDERS  
IN THE HORSE

Robert H. Whitlock, DVM, PhD

Therapeutics of gastrointestinal diseases are most successful when the diagnosis is accurate and the therapeutic agents utilized are in the proper dose, dosage form, interval of administration and given for an adequate time. Additionally, the therapeutic agent should have a low incidence of adverse effects and a wide therapeutic index. Since horses have a wide range of gastrointestinal tract diseases this paper will be limited to a discussion of: 1) acute diarrheal diseases including salmonellosis; 2) colic (abdominal pain); 3) endotoxic shock; 4) verminous arteritis; 4) chronic equine diarrhea; 5) Potomac Fever; 6) gastric and duodenal ulcers; and 7) botulism.

Acute Diarrheal Disease

Acute toxic enterocolitis or acute diarrheal syndrome is a common problem in horses. Approximately 50% of all acute equine diarrheas are attributed to salmonellosis in that Salmonella sp. can be isolated either during the clinical course of the disease from the feces or rectal biopsy material or at necropsy from the colon or cecum. Clostridium perfringens Type A has been recognized as an important cause of acute colitis in Sweden, and more recently in several areas of the United States (44). Probably less than 10% of the cases with acute diarrhea can be attributed to this agent. Most of the other causes of acute equine diarrheal disease (except Potomac Fever) are more difficult to document.

Colitis X is also an acute diarrheal disease in horses in which the exact pathogenesis is unclear. Therapy should be approached in a similar manner to that of any acute diarrheal disease. Treatment for endotoxic shock, which probably is an important component of the Colitis X, syndrome should be included.

A recent trend in equine therapeutics is the non-routine use of antibiotics for acute diarrheal diseases. Five to ten years ago most horses that developed acute diarrheal disease were treated with an antimicrobial agent; today many clinicians have the philosophy that antibiotics are primarily of value in horses with septicemia and/or bacteremia. Clinically it is difficult to recognize which horses might be bacteremic; however, weanlings and yearlings less than 2 years of age are more susceptible to bacteremia. Therefore, it is often recommended to treat acute diarrheal diseases in horses of this age with antimicrobial agents.

Ten years ago the antimicrobial susceptibility of Salmonella was reported to be: penicillin 0%; erythromycin 0%; tetracycline 40%; streptomycin 33%; lincomycin 0%; neomycin 58%; kanamycin 58%; ampicillin 62%; chloramphenicol 96%; nitrofurantoin 96%; gentamicin 100% (37). In the interim period, Salmonella has become more resistant so that today many Salmonella isolates are only partially (50%) susceptible to gentamicin and chloramphenicol. In a

recent study at New Bolton Center with 87 isolates, amikacin was 100% effective, chloramphenicol 39% and gentamicin 40% (7). Surprisingly there was an increased susceptibility to neomycin - nearly 100% during this 6-month period (7). Potentiated sulfonamides had a greater than 50% positive effect but tetracycline susceptibility decreased to 36%. Clinicians expect (often incorrectly) the horse to respond when it is given an antimicrobial agent to which the Salmonella is susceptible. They neglect to consider that extensive lesions may be present in the gastrointestinal tract such as a necrotizing enterocolitis with a pseudomembrane that serves to perpetuate the diarrhea. Therefore, part of the failure to respond to antimicrobial therapy may be the development of intestinal lesions which require time to heal and these lesions are poorly responsive even to the most potent and appropriate antimicrobial agents.

Numerous authors point out the lack of Salmonella isolation from the feces, while a culture of the gut wall may be positive. This fact should emphasize the need for adequate sample size. One gram of feces is minimum and 15-20 grams is recommended. If the culture is negative one cannot "rule out" Salmonella, i.e., it still may be present and only a positive culture is definitive. One early classic report by Graham (18) recovered Salmonella from only 22% of clinically suspected cases of enteric salmonellosis. Similar observations have been made by others as well (8,12).

Probably the most important aspect of diarrheal disease therapy is fluid therapy, both oral and intravenous. Our recommendation is for the use of balanced intravenous electrolytes to correct deficits, especially acidosis and hypokalemia. Horses with diarrhea may absorb orally administered fluids and electrolytes, but if given free choice greatly exacerbate the severity of the diarrhea. We recommend limited access to oral fluids and electrolytes. The amount varies considerably from horse to horse. Overzealous intravenous fluids may also promote the diarrhea. The intensity of the fluid therapy must be adjusted to each patient. Occasionally the PCV may be allowed to increase up to 50% but the creatinine should not be allowed to increase.

Adjunctive therapy would include oral bismuth subsalicylate either as Pepto Bismol® or Corrective Mixture®. The dose is empirical but 8-16 ounces/1,000 lbs QID is often recommended. This preparation has shown proven efficacy with traveler's diarrhea in man (14). The material will cause a dark, almost black stool, so the veterinarian should make the owner aware of this expected change. Powdered activated charcoal also has been recommended (1/2 to 1 lb orally) for acute diarrhea to help bind "toxins" but its efficacy remains unproven. Other protectants and adsorbents such as kaolin, pectin and gum catechu are less commonly used.

The only commercially available Salmonella vaccine is a bacterin which contains antigens against Salmonella dublin and Salmonella typhimurium. It is marketed for cattle but has been used safely in horses (40). Occasionally autogenous Salmonella vaccines are made but are of dubious protective value. New attenuated live vaccines are being evaluated in California and Sweden. These attenuated strains of Salmonella do provide some protection (34).

Antibiotics may also predispose to diarrhea. This was first reported in horses (1) when seven horses were given 15 gm oxytetracycline IV and 5 died of an acute hemorrhagic colitis within 4-12 days of therapy. Coliforms, with Clostridia, were the primary organisms found on fecal culture. Doses of 1-2 mg/kg in stressed ponies and horses also caused acute diarrhea and death (4,11,30).

Owen (28) described ten "stressed" horses, some of which survived in spite of tetracycline therapy. He suggested that the "stressed" horse, which may be a Salmonella carrier, could develop frank disease following tetracycline therapy that would remove the normal bacterial antagonists to Salmonella. Many equine Salmonella isolates are resistant to tetracycline. Tetracycline is concentrated in bile, since the liver is the main excretory route. One can readily appreciate the fact that Salmonella organisms grow rapidly as their bacterial antagonists are inhibited in the gastrointestinal tract (16).

Linerode (23) presented data on the types and numbers of bacteria in the large colon of the horse. When these horses were held off feed or had induced colic the quantitative bacterial counts changed dramatically. If a horse was "stressed" by being held "off feed" and then given different types of feed, tremendous alterations occurred in bacterial flora. These changes would be magnified if an antibiotic such as tetracycline were present to selectively depress some bacteria and allow others to grow, i.e. Salmonella and other toxicogenic bacteria. The altered bacterial population would change and, most likely, decrease the VFA production, which would decrease sodium absorption and tend to result in fluid accumulation in the bowel (2,3). Colitis X may result from this series of events.

Fasting results in a decreased small intestinal absorption of carbohydrate (2) so that more of this rapidly fermentable feed reaches the cecum and colon when the horse is returned to his normal diet. This may result in rapid bacterial fermentation, increased gas production and decreased motility. The end result could be a disastrous colitis. It is recommended to gradually increase feed intake post-operatively to minimize the rapid changes in bacterial flora.

A second but less commonly used antimicrobial agent, lincomycin, has been reported to cause acute colitis in the horse. Perhaps there are few reported adverse effects because of minimal use in horses. Clindamycin is an antibiotic that may be associated with acute colitis in horses and has been well-documented to cause a pseudomembranous colitis in man. Tylosin, penicillin in massive doses, and erythromycin may all, on occasion, be associated with acute colitis. Several outbreaks of colic and acute diarrhea have been associated with monensin-contaminated feed (42).

### Colic (Abdominal Pain)

Colic, a manifestation of abdominal pain, continues to be a common entity requiring therapy by the equine practitioner. The control of pain is necessary to prevent the horse from injuring himself or those in attendance. Complete control of pain can be deleterious as it provides a false sense of security that the patient is recovering when, in fact, surgical intervention may be necessary to alleviate the cause of the colic. Newer potent analgesics may, on occasion, provide this false sense of security.

Nonsteroidal anti-inflammatory drugs are the most popular agents used to manage abdominal pain in the horse. Flunixin meglumine (0.5-1.0 mg/kg) is clearly more potent than phenylbutazone and dipyrone and may provide up to 6 to 8 hours of relief (36). Flunixin, because of its potency, may mask the true cause of the pain and possibly delay surgical intervention since a clinician examining the patient would not be able to discern the severity of the pain. Thus a complete physical examination, including a rectal examination, would be important prior to administering the drug. Some clinicians would use a less potent analgesic, such as dipyrone, on the first examination.

The opioids utilized in the treatment of colic include pentazocine, meperidine, oxymorphone and, recently, butorphanol tartrate (0.05-0.1 mg/kg). All are used on occasion but are not considered the first line of defense. Generally, sedatives are commonly used in these cases. Xylazine is one of the most popular (0.2-0.6 mg/kg), but commonly causes bradycardia, decreased cardiac output and increased urine production (19).

In an attempt to promote evacuation of the intestinal tract, most horses with colic are given 2-4 liters of mineral oil unless there is evidence of gastric reflux. If gastric reflux occurs, removal of the accumulated fluid in the stomach takes precedence and the oil is administered when no reflux is present. In horses with impaction colic, a softening agent such as dioctyl sodium sulfosuccinate is mixed with the oil. Other saline or irritant cathartics such as Epsom salts (magnesium sulfate), Glauber's salts (sodium sulfate) or danthron are used less commonly. The latter may be effective but may promote dehydration through greater fluid accumulation in the colon.

Sedatives and mineral oil remain the two most commonly used agents in the initial treatment of horses with colic.

### Endotoxic Shock

Another distinct entity often present in horses with acute diarrhea or advanced colic is endotoxic shock. Endotoxic shock may be associated with a variety of gastrointestinal disorders, and often a clinician is faced with a dilemma as to treatment of these cases which are characterized by rapid onset, hemoconcentration and a metabolic acidosis. Clearly the role of endotoxins in acute diarrhea is not fully understood. Endotoxic shock itself contributes little to the pathogenesis of the diarrhea. However, it may contribute to many of the biochemical changes associated with acute salmonellosis but not the profuse watery diarrhea. Experimentally, most horses given sub-lethal amounts of endotoxin only develop transient loose stools, not fulminating projectile diarrhea (9).

In one study 5 horses were given *E. coli* endotoxin at 1 mg/40 lb. At 2 hours post-endotoxin each horse received lactated Ringer's slowly intravenously and 2 of the 5 horses received a pulse dose of 5 mg/lb of prednisolone sodium succinate. Clinical signs and biochemical parameters were monitored, including electrolytes, acid-base balance and total plasma proteins. There was no apparent clinical benefit associated with the use of prednisolone and no demonstrable differences in the chemistry or hematology (39). One horse died of a ruptured diaphragm. The results of this study are similar to others published in which the evidence for corticosteroid efficacy in the therapy of endotoxic shock is meager or anecdotal.

Other drugs are continuing to be evaluated for endotoxic shock. These include some of the vasoactive drugs such as alpha-adrenergic blocking agents (e.g. phenoxybenzamine) and dopamine. Some results are encouraging but in order to use these drugs clinically the horses must be rehydrated since the decreased blood pressure associated with these drugs exacerbates any hypovolemic state.

Nonsteroidal anti-inflammatory drugs also have been investigated as aids for colic. There is some evidence that drugs such as flunixin are effective in ameliorating the clinical signs associated with toxic shock but may not alter survival rate (27). Both flunixin and phenylbutazone mask the clinical signs and may delay surgical intervention necessary to correct the primary lesion, i.e., strangulated bowel. The drugs in this category should be used judiciously because of the "masking" effects.

Coincident with the increased use of nonsteroidal agents is the greater recognition of the clinical signs associated with toxicity of these drugs. Some of this early work goes back to the Veterinary Record in 1975, when Dr. Eno reported that ponies given 10 mg/kg of phenylbutazone for 7-10 days developed anorexia, depression, edema and oral ulceration. A variety of clinical syndromes are now recognized in horses receiving toxic doses of nonsteroidal drugs. Hypoproteinemia may occur in as little as five days; the protein decreases from a normal of 7.5 gm/dl to less than 5 gm/dl by Day 10 in many horses. Toxic levels of the drugs cause necrotizing enterocolitis and ulceration, especially in the large intestine and cecum. If the nonsteroidal drugs are withdrawn the lesions usually resolve over a period of weeks or months (35).

A recent novel approach to the treatment of endotoxic shock is the use of antisera against endotoxin. A South African report claimed that horses with a variety of infectious septic conditions responded to the antibody produced by a mutant strain of *E. coli* (17). Another report found greater survival rates in humans with gram-negative bacteremia and shock treated with post-immune antisera compared to similar patients receiving pre-immune sera (45). The sera were obtained from vaccinated human volunteers. Both groups of patients also received a wide variety of therapeutic agents in an attempt to correct the condition.

### Verminous Arteritis

Verminous arteritis is an important consideration in the differential diagnosis of many equine abdominal disorders. Although the entity is considered to be relatively common, the definitive diagnosis is difficult, if not impossible. Preliminary studies designed to evaluate which clinical or laboratory findings might best assist confirmation of a diagnosis of verminous arteritis failed to identify a specific and sensitive factor related to the disease (5). Most equine veterinarians share the opinion that propantheline bromide (15-30 mg/1,000 lbs) intravenously will enhance the diagnosticians' ability to palpate deep internal organs and will significantly reduce the risk

of a rectal tear (Richardson, 1983). The relaxation of the rectal musculature can be further enhanced in the animal sedated using xylazine (0.1 to 0.2 mg/kg). If fremitus can be detected by palpation, or if the history and clinical signs support a diagnosis of verminous arteritis, then a choice has to be made between ivermectin, fenbendazole or thiabendazole. Thiabendazole at 440 mg/kg administered orally on two successive days kills early fourth-stage larvae. Albendazole administered orally at 25 mg/kg three times daily for five days kills migrating larvae permitting resolution of the verminous arteritis (31). Although effective as an anthelmintic, serious side effects do occur and the drug has not been approved for horses. Recently, ivermectin (200 µg/kg intramuscularly) was reported to be highly effective against both early and late stage larvae (33). Ivermectin seems equally effective given orally or intramuscularly (20). Fenbendazole given for 3 days orally at 50 mg/kg or for 5 days at 10 mg/kg was reported to be highly effective against both early and late fourth-stage larvae of Strongylus vulgaris. In as much as an effective safe treatment is available for this relatively common condition, many clinicians treat horses on an empirical basis. If the clinical signs may be attributable to verminous arteritis, then a larvicidal drug is given. If the horse responds, credit is given to the larvicide; if the clinical signs persist beyond 1-3 weeks, alternative disorders are to be seriously considered.

### Chronic Equine Diarrhea

Chronic diarrhea continues to frustrate equine practitioners since the cause remains obscure and the treatment is often ineffective. Early reports suggested an association of chronic equine diarrhea with protozoal infections such as Trichomonas equi or Trichomonas fecalis (6,21). There is now good evidence that trichomonads occur in the feces as a result of wash-out or increased flow rate through the intestinal tract from the cecum to the anus and are not responsible for the diarrhea (13). However, when these horses are treated with a drug such as iodochlorhydroxyquin (Rheaform<sup>®</sup>) by E.R. Squibb & Sons Inc., the diarrhea will improve in consistency (often returning to normal). Horses with chronic diarrhea were found to have an increased fecal concentration of isobutyrate (26). Horses that were treated with iodochlorhydroxyquin (10 gm/day/p.o.) reduced to nearly normal the levels of isobutyrate, suggesting abnormal colonic fermentation may be involved in the pathogenesis of the chronic diarrhea. However, when the treatment is discontinued the diarrhea often recurs even if the drug dosage is gradually tapered off over a period of weeks. Subsequent research has found the isobutyrate to be 1,2-propanediol, not isobutyrate (Palmer, unpublished data). Cecal infusion with 1,2-propanediol did not cause diarrhea although the concentrations of 1,2-propanediol in the feces exceeded those levels found in the natural disease. Thus although iodochlorhydroxyquin seems to be effective in many horses with chronic diarrhea the mechanism of action is obscure.

Transfaunation with cecal contents or fecal extracts are commonly considered but rarely result in improvement of fecal consistency. Additionally, oral drenching with cultured yogurt or buttermilk has proven ineffective in the author's experience, despite the occasional anecdotal report of success.

## Potomac Fever

Potomac Horse Fever is a specific disease of adult horses which was first recognized in Montgomery County, Maryland, in 1979. Affected horses have a variable fever, loss of appetite, depression and a diarrhea which varies from slight to a life-threatening enterocolitis. The severity of clinical signs varies from a transient fever and depression without diarrhea to hypovolemic shock due to severe diarrhea and death (41). Erlichia sennetsu, the causative agent, is poorly responsive to any currently recognized therapeutic agent. Tetracycline will block the infection temporarily (38).

As with other equine diarrheal diseases, supportive therapy, especially fluid replacement, is critical for good patient management. During the summer of 1983 a variety of therapeutic agents were utilized in an effort to minimize the mortality associated with Potomac Fever which is generally 30%. A summary of the therapeutic regimens employed in 59 affected horses and the outcome of each is listed below.

<u>Drugs</u>	<u># Treated</u>	<u>Survival</u>
Antibiotics:	39	64%
a) Trimethoprim-Sulfa	25	76%
b) Penicillin	18	50%
c) Gentamicin	5	40%
Nonsteroidal anti-inflammatory Drugs:	41	56%
a) Flunixin meglumine	35	57%
b) Phenylbutazone	33	54%
Other:		
a) Bismuth subsalicylate	27	3%
b) Heparin	23	78%
c) Atropine	5	40%
d) Corticosteroids	20	50%

Combinations of therapeutic agents seem to improve the survival in affected horses; however, the numbers are small in each group:

<u>Drugs</u>	<u># Treated</u>	<u>Survival</u>
Trimethoprim-Sulfa and Heparin	13	85%
Trimethoprim-Sulfa and Nonsteroidal anti-inflammatory drugs	16	69%
Trimethoprim-Sulfa, Nonsteroidal anti-inflammatory drugs with Heparin	9	89%
Trimethoprim-Sulfa, Heparin and Bismuth subsalicylate	5	80%

Currently an antimicrobial agent such as trimethoprim-sulfa, heparin 40 IU/kg IM, with nonsteroidal anti-inflammatory drugs and fluid replacement seems to be the best combination. The horses should not be stressed by riding or work. Most horses will recover completely except those that develop laminitis, which can be a severe, life-threatening complication.

#### Gastrointestinal Ulceration

Gastrointestinal ulceration, especially involving gastric or duodenal ulcers, is becoming a recognized entity in horses. There are three clinical syndromes associated with this disease process which include:

- a. clinically silent type, recognized only at necropsy.
- b. perforating gastric or duodenal ulcers with acute diffuse peritonitis, unresponsive to therapy since they are not recognized until peritonitis occurs, at which time therapy is ineffective.
- c. duodenal ulcers with stricture of the duodenum.

Foals in the last category are clinically recognized by increased salivation (froth on the lips is typical) and incessant chewing movements. The lesion at necropsy is one of stricture and decreased outflow from the stomach with resultant gastric distention.

Commonly used drugs for gastric and duodenal ulcers include cimetidine at 300-600 mg IV QID, or orally TID. It does not seem to alter bowel function but inhibits pentagastrin- and meal-stimulated gastric acid secretion in man (10,15). Ranitidine is approximately four times more potent than cimetidine and can be given twice a day in smaller doses of 150 mg. There seems to be fewer side effects in humans with ranitidine than with cimetidine. Protectants such as bismuth subsalicylate, aluminum hydroxide and sucralfate (Carafate®), a basic aluminum sucrose sulfate, are used concurrently with the H<sub>2</sub> blockers. Sucralfate, given orally, provides added protection by inducing a local protective mechanism over the area of the lesion. The dose of 1-2 gm orally 3-4 times per day is extrapolated from the human dose. For maximum therapeutic benefit an H<sub>2</sub> blocker and sucralfate should be employed together since their mechanisms of action are quite different. Studies on human patients would suggest that both sucralfate and cimetidine result in similar clinical responses when employed in the treatment of gastric and duodenal ulcers (29). Until further research is completed in horses we cannot be sure of the dose or safety. However, it seems reasonable to follow the recommendations used in man.

### Botulism (Toxicoinfectious)

Toxicoinfectious botulism is considered to be a gastrointestinal intoxication of foals and adult horses. Previously the treatment for this disease was intravenous fluids, force-feeding of a nutrient gruel, slinging the horse and the use of stimulant drugs: neostigmine, 4-aminopyridine or 3,4-diaminopyridine. Stimulant drugs result in improved muscular tone for a short period of time and then the horse will often relapse. In foals botulism, or the "Shaker Foal Syndrome," occurs most commonly in fast-growing foals between 2 to 12 weeks of age. It is a sporadic, non-contagious disease. Foals are often presented with a neuromuscular weakness and an inability to swallow or nurse normally.

Recently Clostridium botulinum Type B toxoid, developed by the Michigan Department of Public Health, has been shown to be safe and effective in producing a protective antibody. The initial regimen should consist of 2 ml intramuscularly at four week intervals. Pregnant mares should be re-vaccinated 6-8 weeks prior to foaling to increase the colostral antibody concentration. This vaccination protocol has resulted in a decreased incidence of "shaker" foals as the protective antibody is present in the colostrum and passed to the foal (22). However, a more recent development is the use of passive antibody (hyperimmune serum) for Clostridium botulinum Type B administered intravenously. This will usually prevent further progression of clinical signs, at least after 12-16 hours, and then with intensive nursing care most of these horses and "shaker" foals improve, especially those who are not recumbent. Prior to the use of antiserum the mortality rate was over 60-80%. Now 80% or more survive, suggesting the antiserum is a marked improvement in therapeutic regimens for the treatment of toxicoinfectious botulism (40).

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