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# Gastrointestinal Diseases of Foals

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## DIARRHEA IN FOALS

Diarrhea has been claimed to occur in 70 to 80 per cent of foals within the first 6 months of life,[70] most frequently in the first weeks of life. Although the morbidity may be quite high, the mortality is very low. The majority of affected foals have a transient self-limiting diarrhea, but when it is not self-limiting or it is severe, the fatality rate can be high.

### Foal Heat Diarrhea

By far the most common diarrhea in foals occurs at 6 to 14 days of age. It is self-limiting and frequently referred to as foal heat diarrhea.[31,36,37,62,70,75] Many possible etiologies have been proposed including hormonal changes,[36,37] changes in milk composition,[27,31,36,70] coprography,[31,36,37] ingestion of genital discharges,[31,36,37] ingestion of roughage and irritants,[31,36] strongyloides,[31,36,37,75] and physiologic changes of the developing intestinal tract.[36,37,75]

Changes in milk volume or composition associated with early lactation or brought about by hormonal changes during the mare's estrus period are commonly thought to be responsible for the diarrhea. However, there is no change in milk volume or composition.[31,70] Milk production may actually decrease rather than increase near day nine post partum; thus, there is unlikely to be excess consumption.[31] In addition, foals raised on an artificial diet with constant composition and volume, developed a self-limiting diarrhea between 9 to 13 days of age that was indistinguishable from foal heat diarrhea.[62]

Likewise, there is no evidence to support coprophagy, ingestion of roughage, and ingestion of sand and other irritants as the cause. There is also little proof that infection with *Strongyloides westerii* is a major cause of foal heat diarrhea.[9,33–35,70] There was no significant

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difference in the incidence of foal heat diarrhea in infected and non-infected foals.[9] In addition, a prospective study using ivermectin found that despite prevention of a patent infection there was no effect on the development of foal heat diarrhea.[33]

Although individual cases may be caused by any of the proposed etiologies, the majority of cases are likely to be a response to a physiologic change in the intestinal tract. Like other neonates, the foal is probably born with an immature intestinal tract[39] that is well adapted for a milk diet. The large intestine receives little ingesta that requires bacterial fermentation before absorption. Buffering mechanisms for colonic fermentation (ileal chloride/bicarbonate exchange) and for absorption of fermentation by-products are probably poorly developed and are certainly not needed in a foal on a milk diet. However, as the foal explores its environment and begins to eat less digestible material, such as grain, hay, and straw, its large intestine must adapt by developing the necessary flora for bacterial fermentation and the mechanisms needed for efficient absorption of the byproducts. If the colon contains a relative excess of such substrate before the absorptive mechanisms are fully developed, diarrhea may result. The transient nature of the diarrhea may reflect rapid functional maturation of the large intestine. The period of diarrhea is approximately equal to the epithelial generation time.

Foal heat diarrhea is soft to watery, but not profuse. The foal's general attitude, appetite, temperature, and other body systems are normal.[31,36,37,75] Because of its transient nature and possible underlying physiologic basis, most cases of foal heat diarrhea should be left untreated. Oral antibiotics or antiperistaltic agents are contraindicated. However, the clinician should perform a complete physical examination and monitor the progress of the patient with periodic re-examinations to insure that the initial diagnosis is correct. Many of the more serious forms of foal diarrhea can initially mimic foal heat diarrhea.

### Nutritional Diarrheas

Foals have a very inquisitive nature and express this through what appears to be unselective feeding during the first month of life. This sometimes results in ingestion of irritating substances or sudden dietary changes, which may lead to diarrhea.[70]

The large intestine may not be able to adapt rapidly enough to ingestion of large quantities of fibrous material, such as grain, forage, and feces, and diarrhea may result.[36,37,70,75] Contrary to popular belief, the common practice of coprophagy is not a source of parasites, for the fresh feces ingested do not contain infective larval stages.

Excessive amounts of milk may be ingested if the mare produces a relative excess of milk or when the foal is reunited with the mare after a brief separation. It also may occur when milk is administered by bottle or via nasogastric tube. The excess amount of milk overwhelms the absorptive capacity of the small intestine and an unusually large amount of incompletely digested milk is presented to the

large intestine. Abnormal fermentation and inefficient absorption results in diarrhea.

Occasionally, foals consume inordinate amounts of sand and dirt, which results in irritation of the intestinal tract and diarrhea.[36,37] This is best demonstrated by finding excessive amounts of geosediment in the feces. Once the habit of eating such material has been established, it is difficult to discourage. One should remove the opportunity so that it can only be practiced occasionally.

Malabsorption is a common problem in foals; however, it is almost always transient and associated with viral diarrhea. Specific carbohydrate intolerances are quite rare, but have been reported.[36,37] The initial damage in these cases may, in fact, have been secondary to viral infection; for some reason, however, the intolerance persists. Because lactose is the primary milk sugar, lactose intolerance will cause significant diarrhea in foals. Lactase deficiency can be demonstrated by comparing glucose and lactose absorption curves.[37] The standard glucose absorption test (1 gm per kg after a 12-hour fast) should be performed. If a normal peak is found, the same procedure should be followed replacing glucose with twice the weight of lactose, for lactase enzymatically splits lactose into glucose and galactose. If the foal is not a malabsorber, the glucose absorption curve should be normal. However, if the foal has a lactase deficiency, the lactose absorption curve should be flat.

**Parasitic Diarrheas**

One of the most common parasites of foals is *Strongyloides westerii*[9,33–37,70]; however, it probably rarely causes diarrhea. The source of infection in most foals is mare's milk. The period of heaviest shedding in milk occurs 2 to 3 weeks after parturition.[34,36] Ingestion of massive numbers of larvae, at least 100 times the level in mare's milk,[9] are required to produce diarrhea.[34] It is highly unlikely that a foal would receive a sudden bolus of such a large number of infective larvae, and the small numbers constantly ingested over a long period of time are apparently harmless in most cases.[9]

Several drugs have been found to be effective in treating *Strongyloids westerii* in the foal. Ivermectin at a dose of 200 μg per kg has been reported to be successful.[33] Also, thiabendazole at 50 mg per kg,[36,37] cambendazole at 20 mg per kg,[36,37] and oxibendazole at 10 mg per kg[37] have all been found to be successful. Whatever the role of *Strongyloides westerii*, the clinical observation has been made that the treatment with thiabendazole at 50 mg per kg occasionally is followed by cessation of diarrhea in foals.[35] In these cases, the thiabendazole may be playing some therapeutic role other than that of an anthelmentic.

Another potential cause of foal diarrhea is *Strongylus vulgaris*. Because of its long prepatent period, practitioners often do not think of *Strongulus vulgaris* as a disease of foals. However, larvae penetrate the mucosa by day three postingestion and can be found in the ileocecocolic artery by day 14 to 21. Thus, if a foal is exposed to a

heavily contaminated environment early in life, it may show signs of the intestinal phase in the first 2 weeks of life and signs of the arterial phase within the first month of life.

During the early intestinal phase, the larvae penetrate and molt to the L-4 stage in the mucosa. Associated with this stage of infection a generalized arteritis occurs in the submucosa and serosa, resulting in marked inflammation. The intestinal phase is associated with pyrexia, anorexia, dullness, abdominal pain,[19] and diarrhea.[36,37,39] Because this period probably does not last more than a week, diarrhea from one exposure should be short-lived.[37]

The arterial phase begins about 3 weeks after infection and is associated with thrombosis, thickening of the intima, and narrowing of the lumen of the ileocecocolic artery. This period may also be associated with pyrexia, anorexia, depression, diarrhea, or constipation and colic.[46] If the conditions are correct, the diarrhea may become chronic. The author has observed foals who developed diarrhea within the first 2 weeks of life, continued with a chronic watery diarrhea for 2 to 3 months, and had severe verminous lesions of the ileocecocolic artery and its branches. Such foals are refractory to symptomatic therapy and have no other detectable underlying etiology at necropsy.

Diagnosis of *Strongylus vulgaris* diarrhea in the foal may be difficult. A presumptive diagnosis may be made from signs and observation of poor management. The neutrophilia, eosinophilia, and increase in beta globulins associated with experimental infections in foals[19] may be seen in naturally exposed foals who have a massive exposure to the parasite early in life. However, because most foals have repeated exposure, these changes are not usually evident. A therapeutic trial with thiabendazole (440 mg per kg on two consecutive days), fenbendazole (10 mg per kg on five consecutive days), or ivermectin may be rewarding in suspicious cases. Occasionally, repeated larvicidal therapy appears to be helpful. Although most of the damage can be repaired leaving only fibrosis,[19] the repair process may take a month to 6 weeks.

### Viral Diarrhea

Rotavirus,[14,15,20,23–26,32,37,40,56,63,67,69,70,76,77] coronavirus,[8,20,70,73] and adenovirus[16,27,64,75] have all been associated with diarrhea in foals. Although the role of rotavirus has been clearly demonstrated, the roles of coronavirus and adenovirus need further investigation.

There have been several reports of coronavirus-associated diarrhea in foals,[8,20,73] but the role of the virus is not clear. It is likely that adenovirus is not a primary agent but may complicate infection by other pathogens or take advantage of immunoincompetence.

Rotavirus is a commonly reported cause of foal diarrhea.[14,15,20,25,32,40,56,63,65,69,70,77] Up to 30 per cent of foals with diarrhea have been reported to have rotavirus particles in their feces, and nearly 100 per cent of adult horses have antibodies to rotavirus.[15] Rotavirus diarrhea appears to occur as an epidemic,[20,61,63,69] with a

high percentage of the foal herd affected.[15,20,56,63,69,77] The source of the virus in such outbreaks is probably adult subclinical shedders.[15,56,77] The virus can also be shed subclinically in foals for up to 8 months.[14] Because of its ability to survive up to 9 months in the environment[15] and its widespread prevalence in the equine population, epidemics are most likely to occur when population pressures and management practices favor heavy contamination of the environment. Because of the widespread nature of the pathogen, it is likely that most mares produce some protective antibodies in their colostrum; however, this antibody will not be protective against an overwhelming infective dose.[77] Although only a small percentage of foals will show clinical signs, it is very likely that 100 per cent of the foals on the property are infected during epidemics.[77]

Most foals with rotavirus diarrhea are less than 2 months of age,[15,32,56,65,69] and frequently less than 1 month. The first signs are depression and failure to nurse, which are usually followed in 12 to 24 hours by profuse, nonfetid, watery diarrhea.[32,40,63,65,69,77] Fever is variable, but when it occurs may be associated with secondary bacterial infection.[77] Weight loss and debilitation may occur during and after the diarrhea.[77] Reported leukopenias are probably not directly a result of the rotavirus infection.

Infection by rotavirus is thought to be limited to the small intestine. The virus invades the absorptive epithelial cells on the villus.[74] It destroys cell function and shortens its life, resulting in decreased villus size, compensatory proliferation of crypt cells, and rapid migration of the cells from the crypts without opportunity for maturation. Thus, there is not only a loss of absorptive epithelial cells but also a hypertrophy of crypt secretory cells with the net result of decreased absorption of substrates and increased secretion.[41] Although the villus-to-crypt ratio may be decreased for up to 21 days, signs usually do not persist for this period of time.[77] With the loss of function of the small intestine, the neonate whose large intestine has not developed to a point where it could compensate would be likely to show more severe signs than a weanling.[4]

There are numerous methods for detecting rotavirus in the feces including electron microscopy, immunoelectron microscopy, immunofluorescence, enzyme immunology, and radioimmunoassay. Isolation of the virus is difficult and unnecessary due to the specificity and sensitivity of existing detection tests. Electromicroscopic detection of rotavirus requires at least $10^5$ viral particles per ml.[15,24] Most samples with $10^6$ virus particles should not be missed on electron microscopy, and those with $10^8$ are easily diagnosed, providing a rapid diagnostic test in such cases.[24] The enzyme-linked immunoassay technique (Rotazine)* is an equally sensitive and rapid detection method that has the advantage of being much less expensive.

*Rotazine. Abbott Laboratories, Chicago, Illinois.

This test takes advantage of a group-specific antigen common to rotaviruses from all species (except pararotaviruses). Thus, it can be used to identify rotavirus from numerous species. There is good agreement with the Rotazine test and electron microscopic examination of foal feces.[14]

As diagnostic tests to detect viruses become more sensitive, we must become careful in our interpretation of the results. It is commonly assumed that if a pathogen is found in the feces of an animal with diarrhea, it is causing the diarrhea. Conversely, it is assumed that if a pathogen is not found in the feces of an animal with diarrhea, it is not causing the problem. Neither is true. Because of the apparent high incidence of subclinical infection,[77] the virus may be detected even though it is not causing clinical signs. A further complicating factor is infection by multiple pathogens. In calves and pigs, rotavirus infections are often complicated by concurrent infections with bacteria such as *E. coli, Salmonella,* or other viruses, such as coronavirus.[77] In foals, infection has been concurrent with *Salmonella* infection.[23,69] Thus, the search for possible pathogens should not stop with the detection of one. Diagnostic attempts should be made during the first few days of illness, because viruses are often shed only early in the disease, even before the onset of diarrhea.[56,63]

Although attenuated rotavirus vaccines made for other species have been used in foals,[23,76] there is little indication that they afford protection. Despite the presence of common group-specific antigens among all the rotaviruses,[14,76,77] the degree of cross-protection between rotaviruses is unreliable and probably depends on the individual's immune response.[77] "Vaccination" with foal rotavirus will not protect calves against natural infection by the bovine virus.[26,25] One cannot rely on vaccines made for other species to protect foals against rotavirus.

The most effective way to prevent rotavirus diarrhea in foals is to control factors that lead to epidemics with good management and preventative health measures. As the virus is probably found in the environment of most foals, it is exceedingly difficult to prevent exposure. Most foals exposed to low levels of virus develop subclinical infections. When population pressures arise, as with heavy density management, contamination of the environment may become heavy enough to lead to epidemics.[63] Although colostral antibodies would be produced by a mare exposed to this environment, a high dose of virus could be expected to overcome this protection.[77]

### Bacterial Diarrheas

Potential bacterial causes of foal diarrhea include *Salmonella* spp., *Escherichia coli, Clostridium* spp., *Rhodococcus* (*Corynebacterium*) *equi,* and *Campylobacter* spp. Diarrhea is also frequent secondary to septicemia caused by various bacteria including *Actinobacillus equuli, Salmonella* spp., *E. coli,* and *Streptococcus* spp.

***Salmonellosis.*** One of the most common and serious causes of bacterial enteritis in the foal is infection by *Salmonella* spp. Since

the first description in 1919,[28] equine salmonellosis has become a well-established disease syndrome.[6,10,30,44,58–60] Over 1700 serotypes have been identified. The microbe attacks all mammals, most vertebrates, and many invertebrates and is widespread in nature.[43] The most common serotype in horses is *S. typhimurium*.

The most likely source of infection for the foal is another horse, although other animals or the environment may also serve as sources. Because the equine shedder shares the foal's environment, it has the best opportunity to contaminate of the foal's environment, thus posing as the most likely source. Approximately 10 per cent of horses have been or are asymtomatic *Salmonella* shedders.[44,48] Because of their intimate association, the most likely source of contamination of the foal's environment is the mare. Indeed, in the majority of cases of foal salmonellosis the mare can be found to be shedding the microbe. Whether the mare is the original source or the foal is the source for the mare is not clear, however.

There are several important determinants of infection, including exposure dose, virulence of the bacterium, immune status of the host, and level of stress the host is experiencing. Although mature horses with acute salmonellosis often have a history of severe stress,[47] foals without demonstrable stress seem to be highly susceptible. The major role of stress in adult horses is likely to be a change in the horse's normal intestinal flora, but the foal may be more susceptible because the flora is just developing.

Clinical syndromes of salmonellosis in the foal may range from a mild enteritis resembling foal heat diarrhea to fulminating septicemia. Enteritis is the most common clinical manifestation. During the initial 24 to 48 hours of disease, the foal appears depressed, may be febrile, shows some mild abdominal pain, usually has an increased heart rate and "toxic" mucous membranes. Diarrhea, ranging from cow-like to watery and projectile, often begins sometime after the initial signs of illness. The feces often have a characteristic foul odor, probably associated with the putrification of protein that is lost through the intestinal tract. The diarrhea may be infrequent or profuse and dehydrating and may last only a few days or 3 to 4 weeks or longer.

A septicemic form that is difficult to distinguish from *E. coli* and streptococcal septicemias may occur in foals as young as 12 hours of age. In such cases, it is rare to note an enteritis. Foals less than 6 months of age seem to be particularly prone to bacteremia even when the only other sign is a mild diarrhea. The most common sequela to the bacteremia is a septic physitis. Occasionally, pneumonia, nephritis, and meningitis may be seen.

Chronic diarrhea is rarely caused by *Salmonella*, although occasionally a foal may have diarrhea for 1 to 2 months. If the enteritis occurs during an important period in the development of the foal's flora, the disturbance of flora may perpetuate the diarrhea for prolonged periods of time. Such foals neither shed *Salmonella* nor have active *Salmonella*-induced lesions. On rare occasions, the damage to

the intestinal tract may be severe enough to cause chronic structures or perforations, which may lead to chronic manifestations of colic, abdominal distension, and poor growth without diarrhea.

Despite laboratory findings characteristic of salmonellosis, there is a great deal of individual variability and no laboratory test is diagnostic. Leukopenia (less than 3600 cells per μl) is primarily due to a neutropenia and, frequently, a lymphopenia. The total leukocyte count can be as low as 600 cell per μl. Hyponatremia (112 to 124 mg per dl), hypochloremia (80 to 90 mEq per L), hypokalemia (1.0 to 2.4 mEq per L), hypocalcemia (8 to 10 mEq per L), acidemia (bicarbonate 8 to 16 mEq per L), and an azotemia, as reflected by an increased creatinine, are common. Although occasionally there is tubular necrosis or nephritis, the azotemia is initially prerenal and the creatinine decreases with rehydration.

Diagnosis of salmonellosis is best achieved through fecal culture. Ten to 15 g of feces should be placed in adequate enrichment media (ratio 1:10). When fecal material cannot be obtained, rectal swabs can be used but are less sensitive. Because *Salmonella* is not consistently shed during the disease, multiple cultures are often needed before a positive result is obtained. When there is a high index of suspicion, at least five cultures should be obtained.[48]

General guidelines on therapy of foal diarrheas will follow later; however, because of the controversy, a few comments will be made regarding the use of antibiotics in salmonellosis. Appropriate antibiotics will not shorten the course of *Salmonella*-associated diarrheas, and inappropriate antibiotics may disrupt the normal flora and allow *Salmonella* to grow and colonize more successfully. Plasmids carrying resistance factors are readily transferred, not only between *Salmonella* spp. but also between *Salmonella* spp. and other enterobacteriaceae such as *E. coli*.[66] Thus, if the plasmids exist in the environment, especially under the pressure of heavy use of antibiotics, they may easily be transferred to the pathogen.

Although antibiotics may not shorten the course of diarrhea, in cases of bacteremia, antibiotics may prevent secondary infections at the physis and other locations and, therefore, may afford some benefits. Thus, foals with salmonellosis may benefit from appropriate antibiotic therapy. However, because of the high incidence of resistance to commonly used antibiotics, a sensitivity must be run on each isolate as it is obtained. It should always be remembered that the production of resistant *Salmonella* spp. is a hazard to other animals, including man.[48] The implications of producing multiple resistant bacterial strains in a zoonotic disease can be great.

The probability of infection is inversely proportional to the quality of management. It is important to minimize stress. Sound feeding and parasite management practices should be followed. The breeding stock should not be in contact with transients, and there should be separate facilities for racing and showing animals to eliminate physical contact with the breeding animals. Decreasing the traffic between animals and good hygienic practices are the most

important factors in decreasing the probability of *Salmonella* outbreaks in foals.

***Other Bacterial Diarrheas.*** *Escherichia coli* is a frequent cause of neonatal diarrhea in other species, but enteric colibacillosis has not been documented in the foal.[11,37,70,75] Although *E. coli* infects foals, it frequently causes septicemia that may or may not have associated diarrhea.[11,37,75] Specific enteropathogenic *E. coli* have not been identified in the horse.[37,70] Although it is likely that they occur, they probably are not an important cause of diarrhea in the foal. Good colostrum management, clean foaling areas, and lack of overcrowding are all factors that contribute to a low probability of infection. Because enteropathogenic serotypes have not been identified, it is nearly impossible to make a specific diagnosis of enteropathogenic colibacillosis in the foal.

*Clostridium perfringens* and *Clostridium welchii*, types B and C, may produce a necrotizing hemorrhagic enteritis in 1- and 2-day-old foals.[70,75] Cases are usually sporadic, but an outbreak on one farm has been reported.[70] Occasionally, foals die without prior signs and are found to have intestinal hemorrhage and necrosis. Other foals may become profoundly depressed, show marked systemic signs, pass blood-stained diarrhea, become moribund, and die within 48 hours. Because *Clostridium* spp. may be found in the normal intestinal tract of animals[45] and in soil,[45] isolation of *Clostridium* spp. is not necessarily diagnostic of the disease. Finding specific lesions and the presence of toxin are more specific.

During the last few years, there has been an increased interest in the role of *Campylobacter* in diarrhea with conflicting information about its role in foal diarrhea.[5,50] Further research is required to determine its importance in foal diarrhea. *Rhodococcus equi* may, on occasion, cause diarrhea in older foals[12,70] but has not been a recognized problem in neonates.

### Antibiotics

Antibiotics, most commonly oxytetracycline and lincomycin[36] and more recently erythromycin, penicillin, and trimethoprim-sulfa, are occasionally associated with diarrhea in horses. The antibiotics probably induce a change in intestinal flora. Aminoglycosides, because of their effect on enterobacteriaceae and their lack of effect on anaerobes, coupled with the lack of absorption when administered orally, are likely to cause radical imbalances of the intestinal flora and should not be used to treat diarrhea.

## THERAPY FOR FOAL DIARRHEA

The most important therapeutic consideration in all diarrheal diseases is fluid balance. When acute diarrhea is dehydrating, the loss of water is usually isotonic and associated with hyponatremia, hypochloremia, hypokalemia, hypocalcemia, and acidosis. Increased

thirst and availability of electrolyte-free water help contribute to the electrolyte imbalance. If dehydration is mild, the foal may be able to correct the dehydration and electrolyte imbalances when offered free choice fresh water and water containing electrolytes. The water containing electrolytes should be isotonic. The following formula has been successfully used in underdeveloped countries when treating children with acute diarrhea: 90 mEq per L sodium + 80 mEq per L chloride + 20 mEq per L potassium + 30 mEq per L bicarbonate + 2 per cent glucose.[49] Some foals will refuse to drink the solution when glucose has been added. Fresh water should be available at all times, because some foals refuse water containing electrolytes. Mare's milk is also a source of water and electrolytes.

If the diarrhea is severely dehydrating or if the neonate is weak or for some reason unwilling or unable to drink, intravenous fluids are indicated. A balanced isotonic electrolyte solution should be used, keeping in mind that the foal may be moderately to severely acidotic and hypokalemic. If the foal has been severely hyponatremic for some time, it should not be given hypertonic sodium-containing fluids such as 5 per cent sodium bicarbonate or isotonic sodium-containing fluids rapidly, because a rapid rise in the serum sodium level may induce neurologic signs and cerebral hemorrhage. If hyponatremia has been a chronic condition, it should be corrected cautiously—not overaggressively.

In general, antimicrobials are overused in foal diarrhea and should not be used unless there is evidence that the causative agent is sensitive to the antibiotic. If the diarrhea is caused by an infectious agent that is not sensitive to the antibiotic, use of the antibiotic may favor colonization by the pathogen. If the diarrhea is a functional problem, then the use of antibiotics may cause imbalances of intestinal flora, which may favor the growth of pathogens and result in secondary bacterial disease. Certainly it is not rational to treat viral diarrheas with antibiotics. Seriously ill foals should be placed on parenteral antibiotics when a bacteremia is likely. However, the use of nonabsorbable oral antibiotics has no place in the treatment of diarrheal diseases in foals.

When specific antidiarrheal drugs are used to combat foal diarrhea, the aim should be to decrease net secretion rather than to decrease the transit rate. Increased transit rate of ingesta through the gastrointestinal tract is a natural defense mechanism of the host; it effectively removes toxins and agents before they are absorbed or can invade. Thus, diarrhea in itself may be therapeutic, and it may be contraindicated to interfere with transit rate. The problem arises when there is massive fluid loss leading to dehydration along with the increased transit rate. Our efforts should focus on decreasing this fluid output, changing net secretion to net absorption. Antimotility and anticholinergic agents should be avoided, but drugs such as bismuth subsalicylate, which may be antisecretory, may be helpful. Bismuth subsalicylate at a dose of 6 oz per 45 kg given two to four times a day, has decreased diarrhea in some cases. Other agents, such as activated charcoal or kaolin and pectin, may also be helpful. If these

agents do not produce a change in the diarrhea within 48 to 72 hours, continued use is not indicated. Nonsteroidal anti-inflammatory drugs may be beneficial in decreasing the secretory component of the diarrhea, but because of their potential toxicity, which may be manifested by gastrointestinal signs, they should be used with caution and moderation.

## GASTRIC AND DUODENAL ULCERS

Gastric and duodenal ulcers in foals are being recognized more frequently. They resemble peptic ulcers in man, which develop in the presence of acid and pepsin.[21] Peptic ulcer disease occurs most commonly in the stomach and proximal duodenum.[21] In foals, frequently both areas are affected simultaneously. Diagnosis is based on a discrete set of signs.

### Gastric Ulcers

Gastric ulcers occur when aggressive factors that may cause damage to the gastric mucosa overcome protective factors that are responsible for the mucosa's resistance to injury.[17,18,21,57] Rooney[55] proposed that physical trauma plays a role and that stones or other geosediment were major initiating factors. Foals under severe stress frequently develop gastric ulcers. The pathophysical connection between stress and ulceration is not clear. Although it has been commonly assumed that adrenal steroids result in ulceration,[29] these compounds have not been found to be clearly ulcerogenic even in pharmacologic doses.[21]

The major protective mechanism of the gastric mucosa appears to lie in the epithelial cell membrane,[21] which has an innate resistance to physical and chemical trauma imparted by low levels of prostaglandins.[54] If prostaglandin levels decrease, ulceration occurs. Nonsteroidal anti-inflammatory drugs may be ulcerogenic because they decrease the prostaglandin level below that required for their protective effect.

Gastric ulcers may be nonperforating or perforating. The former may be subclinical and are frequently found along the margo plicatus at postmortem in foals that have other diseases. Clinical nonperforating gastric ulcers are usually found in this area or may be found in the glandular or nonglandular stomach. Perforating gastric ulcers, which are likely to be a progression of nonperforating ulcers, can also occur in any of these areas. When one ulcer perforates, there are often other nonperforating ulcers present.

The three signs of colic, ptyalism, and bruxism in combination should make the diagnostician's index of suspicion very high for gastric or duodenal ulcers. Other nonspecific signs of nonperforating gastric ulcers include depression, anorexia, tachycardia, tachypnea, fever, decreased borborygmal sounds, gastric reflux, and occasionally diarrhea, which may contain occult blood. In some cases, cranial

abdominal pain can be localized to the zyphoid area by deep abdominal palpation.[29,51]

The signs associated with a perforated gastric ulcer are typically those of diffuse peritonitis. Profound depression, extreme tachycardia (above 120 beats per minute), tachypnea, hypothermia, injected mucous membranes with a blue toxic ring, and abdominal distension are usually found. Some foals will have a history of signs compatible with a nonperforating ulcer for some time before the perforation occurs.

Diagnosis is frequently based on consistent clinical signs after ruling out other possible causes. However, a definitive diagnosis is often difficult without direct observation of ulcers via endoscopy. Solid food should be withheld for at least 12 hours and milk for at least 4 hours before endoscopy is attempted. Even after such precautions, ingesta and gastric secretions may remain in the stomach and can obscure the pyloric and ventral areas of the stomach. Thus, although endoscopy is the ideal procedure, it will not always detect the presence of ulcers. Contrast radiography can also be used, but experience is required in interpreting the results. Examination of gastric fluid for the presence of inflammatory cells might be useful in establishing inflammatory disease of the stomach or proximal small intestine but is not specific for gastric ulceration.

Foals with perforating gastric ulcers have a grave prognosis—the fatality rate approaches 100 per cent. Foals with nonperforating ulcers will frequently recover; however, the course may be prolonged. As in man, complete healing of ulcers probably requires a month or more. Chronic sequelae to nonperforating gastric ulcers are rare, but chronic fibrosis of the pyloric area may interfere with gastric emptying. An abscess formed in this area secondary to a perforated gastric ulcer may have a similar effect.

**Duodenal Ulcer Disease**

Perforating duodenal ulcers follow a course similar to that of perforating gastric ulcers; however, nonperforating duodenal ulcers frequently result in stricture and obstruction of the duodenum, which lead to major problems. A segmental ulcerative duodenitis rather than a small discrete duodenal ulcer, is more commonly found, frequently near the bile duct entrance.[1,38,51,72] The cause is not clear. Because of the apparent clustering of cases, an infectious agent has been sought.[1] Stress and the use of nonsteroidal anti-inflammatory drugs have also been proposed, because it is common in the history. The suggestion that duodenal strictures are congenital and only produce signs when the diet is no longer liquid[38,72] is not supported by histologic examination, which usually reveals that these strictures are secondary to ulcer disease[51] and the fact that signs may be seen as early as 5 days of age.

Bile, an ulcergenic substance,[21] may be important in the pathogenesis of the disease. Epithelial cells of the duodenum normally are very resistant to its effects, partly because of "cytoprotection,"[54] which is mediated through prostaglandins.[54] In the presence of high

levels of nonsteroidal anti-inflammatory drugs, which decrease prostaglandin levels, cytoprotection is lost and bile may cause ulceration. This would explain the segmental nature of the problem and the location. However, nonsteroidal anti-inflammatories cannot be blamed for the disease in every case, because some affected foals have never been treated with these drugs.

Perforating duodenal ulcers occur most frequently in 1-month-old foals; however, they may occur from a few days to 2 months of age. Frequently, the foal has a 24- to 48-hour history of vague signs of pain, bruxism, mild diarrhea, and rolling onto its back with the front legs over its head, followed by a sudden onset of acute septic shock with signs typical of those seen with perforating gastric ulcers. The foal usually dies within 6 to 12 hours.

The chronic form of the disease with the accompanying stricture usually occurs in 2- to 3-month-old foals; however, it may occur in foals as young as a few days of age or as old as 4 months. Frequently, these foals have a history of abdominal pain, poor growth, and pneumonia during the previous 30 days. They salivate excessively, often having white foam dripping from their mouth and nose, incessantly grind their teeth, are depressed, may have a fever, and, although they nurse, are underweight. When one of these foals lowers its head, large quantities of saliva and milk may run out of its nose. Aspiration pneumonia is common. Colic is usually present and most intense after nursing. Draining the gastric reflux may afford temporary relief. Occasionally, the cervical esophagus is notably distended (mega-esophagus) and full of fluid. A fluid wave corresponding to respiration may be seen in the distal cervical esophagus. Passing a nasoesophageal tube will result in removal of fluid from the thoracic esophagus.

Diagnosis of duodenal stricture is often made on clinical signs and physical examination findings. Endoscopy frequently reveals esophagitis, mega-esophagus, and sometimes gastric ulcers, but profuse salivation and excessive gastric fluid often make lesions difficult to see. Contrast radiography is also helpful. The barium remains in the esophagus for prolonged periods of time, especially in front of the heart base and between the heart and the diaphragm. Gastric fluid may be seen refluxing into the esophagus, which reflects loss of tone in the cardia, and the gastric silhouette will be very large with delayed gastric emptying. If no contrast material fills the small intestine within 60 to 90 minutes and there is an absence of distension of the small or large intestine, indicating an ileus, then duodenal stricture is highly likely. Examination of peritoneal fluid will frequently show an increase in protein with a normal cell count.

Frequently, foals with duodenal strictures will be moderately dehydrated, hyponatremic, hypochloremic, hypocalemic, acidotic, and have a prerenal azotemia. Without treatment, the acidosis may become profound, with the blood pH dropping below 7.00. Aspiration pneumonia, which is almost impossible to avoid with a fluid-filled mega-esophagus, may be serious and result in the foal's death. Once the full spectrum of signs has developed, the prognosis is grave,

although surgical intervention with a gastrojejunostomy may be curative.

## TREATMENT OF GASTRIC AND DUODENAL ULCERS

There are two medical approaches that can be used in treating gastric and duodenal ulcers. The traditional approach, which assumes that acid is not only responsible for the ulcer but also retards healing, is to decrease the acid and pepsin contact with the ulcer. The newer approach is based on increasing the resistance of the mucosal cell to injury and returning it to general health.

### Antacids and Antisecretory Agents

The basis for use of antacids is to increase the gastric pH to above 5 to abolish the damage done by the acid and prevent activation of pepsinogen to pepsin. The effectiveness of antacids is not necessarily dose-related but depends on other conditions surrounding their administration.[7,52] If given on an empty stomach, effectiveness will be diminished after 20 to 30 minutes because of rapid gastric emptying,[7,52] regardless of the dose. However, if the antacid is given an hour after a meal, then it is likely to be effective for several hours. When choosing a dose, the concentration is important, for an overdose of concentrated form may lead to diarrhea. The four most effective antacids are sodium bicarbonate, calcium carbonate, aluminum hydroxide, and magnesium hydroxide.[7] Each may cause problems, such as systemic alkalosis with sodium bicarbonate and diarrhea with magnesium hydroxide. For this reason, most manufacturers use combinations. The most effective antacids on the market today are combinations of aluminum hydroxide and magnesium hydroxide.[7,52]

Although gastric $H_2$ receptors have not been identified in horses, antihistamines that block $H_2$ receptors are commonly used in therapy of equine ulcer disease. In man and other animals, it has been shown that these drugs out-compete histamine for receptors on parietal cells,[13,78] inhibiting basal gastric secretion 100 per cent and increasing the pH of the secretion to 5 or above. They decrease food stimulated gastric secretion by 50 to 75 per cent.[13,52,78] The most commonly used $H_2$ blocker is cimetidine (Tagamet),* which may be given intravenously or orally to foals at a dose of 300 to 600 mg, four times a day. The oral form cannot be used concurrently with antacids, for antacids inactivate the drug. A relatively new $H_2$ blocker, ranitidine, has been found in man to be more potent and longer acting than cimetidine[13] in man and is not inactivated by antacids when given orally. It has been used at a dose of 150 mg twice a day in foals. In man, although $H_2$ blockers are very effective in decreasing acid output, their effectiveness is no better than aggressive antacid therapy in speeding the healing of ulcers.[13,22,78] Their efficacy in foals is unproven. Antacids

* Smith Kline & French Laboratories, Philadelphia, Pennsylvania.

and antisecretory agents should be continued for approximately 1 month for complete healing of ulcers.

### Cytoprotective Agents

The new generation of antiulcer medication increases cytoprotection[53] probably by increasing prostaglandin formation or replacing prostaglandins. Sucralfate (Carafate),* a complex of a sulfated sucrose and aluminum hydroxide, in the presence of proteinaceous exudate and hydrogen ions, forms an adherent complex that is an effective barrier to hydrogen ions, pepsin, and bile. Endoscopically, the drug can be seen to adhere only to the ulcer site. This adherent barrier probably is not an important part of its mechanism of action, for it would hold acid and pepsin against the secretory epithelium. Its mechanism of action is more likely stimulation of local prostaglandin production. In man, it has shown good clinical efficacy in limited trials, being as efficacious as cimetidine or aggressive antacid therapy. Like cimetidine, its efficacy has not been proven in the foal; however, because it is not absorbed and is independent of the existence of parietal cell receptor sites, it is more likely to be effective. It is also less likely to be toxic. It has been used at the dose rate of 2 to 4 gm, four times a day in foals.

Other medications that have been recently introduced as antiulcer medications in man and that have shown some promise include colloidal bismuth subcitrate,[68] carbenoxolone sodium, and 16,16-diethyl $PGE_2$.[53] The latter product is a synthetic prostaglandin that is resistant to destruction in the gastrointestinal tract and that has been found very effective in protecting gastric mucosa from damage. It should be helpful in preventing ulcers caused by nonsteroidal, anti-inflammatory drugs; however, the dose required should be quite small, and an overdose may cause side effects such as diarrhea. Its use in foals has not been investigated.

## SUMMARY

Few foals escape gastrointestinal disease during the first weeks of life. Diarrhea is an extremely common problem; fortunately, however, it is usually mild and self-limiting. When it is not, the underlying cause is often an infectious agent, such as rotavirus or *Salmonella* spp. Our understanding of many of the infectious agents causing neonatal diarrhea is far from complete. Gastric and duodenal ulcers are a less common disease of neonatal foals. There has been an apparent increase in the incidence of ulcer disease in foals during the past few years. The most effective way of decreasing serious gastrointestinal disease in foals is through the use of good management practices. Environmental and dietary stress must be minimized, and good hygienic practices should be followed. Unfortunately, the needs of

* Marion Laboratories, Inc., Kansas City, Missouri.

the neonate are often ignored, while attention is focused on the mare during the breeding season.

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