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11 Gastrointestinal Disease

Case 11-1	Colic in the Newborn Foal	Michelle Henry Barton

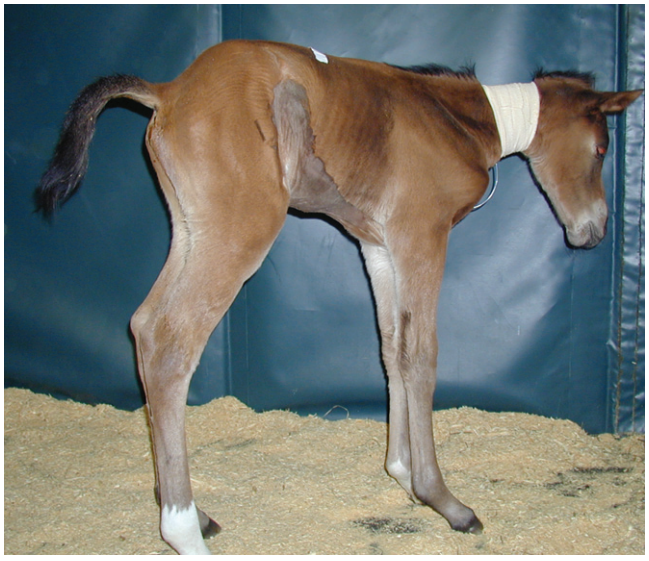

Fig. 11-1 Straining to defecate. '03 RockN'Roll at the time of presentation to the Veterinary Teaching Hospital at approximately 26 hours of age. The foal is exhibiting signs of straining to defecate: raised tail head, slightly arched back, hindlimbs slightly under the trunk. Note the meconium staining on the tail and perineum. The white tape on the foal's back was used as a landmark to serially measure the circumference of the foal's abdomen. Compare this foal's stance to the stance in Figure 11-4.

RockN'Roll, a 12-year-old Thoroughbred mare, foaled uneventfully at approximately 4 PM on April 14, 2004. '03 RockN'Roll stood within two hours of delivery and nursed. He passed meconium at approximately four hours of age, and he seemed bright and alert. On the morning of April 15, the owners found the foal straining to defecate. The local veterinarian was called for further evaluation and found a quiet but alert foal with a normal rectal temperature and heart rate. Meconium staining was noted on the tail. Gastrointestinal sounds were audible on both sides of the abdomen. A digital rectal examination was performed, and firm meconium was palpable in the rectal ampulla. A nasogastric tube was passed. No reflux was obtained, thus 30 ml of dioctyl sodium sulfosuccinate (DSS) was given. In addition, 50 mg of flunixin meglumine was given intravenously and a DSS and water enema was administered. The foal continued to strain and was intermittently recumbent, prompting referral to the University of Georgia's Veterinary Teaching Hospital.

At the time of presentation, '03 RockN'Roll was approximately 26 hours old. The foal was quiet, but tracked the mare well and was interested in nursing. The abdomen was slightly distended, and meconium staining was present on the tail and perineum. Shortly after admission, the foal was observed to raise his tailhead and strain (Figure 11-1). A small amount of urine was passed. The rectal temperature was 100° F, heart rate was 88 beats/minute, and respirations were 40 breaths/minute. Borborygmi were audible on both sides of the abdomen. A nasogastric tube was passed, and no reflux was obtained. A digital rectal examination confirmed the presence of firm meconium at the pelvic inlet. Palpation through the abdominal wall revealed at least a 12-cm segment of bowel in the left caudoventral abdomen that was approximately 3 cm in diameter and contained firm ingesta. Intermittent straining, as well as flank biting, continued. The foal then became recumbent and rolled up onto his back. There were no other significant physical findings. The major problems identified were straining to defecate, mild abdominal distension, acute abdominal pain (colic), and firm feces at the pelvic inlet.

DIAGNOSTIC APPROACH TO COLIC IN NEONATAL FOALS

According to the results of the National Animal Health Monitoring System report on colic in horses in the

United States in 1998 and 1999, the incidence of colic in foals less than six months of age was approximately 18 times less than the incidence in mature horses.[1] However, when considering aliments affecting foals, gastrointestinal tract problems and infection were most commonly reported.[2,3] Because some etiologies of colic are unique in the neonatal period, special consideration must be given to the evaluation of abdominal pain in this age group.

In some respects, the diagnostic approach to colic in neonatal foals is similar to that used in mature horses: rarely will any single fact be useful in determining the exact etiology. However, careful and simultaneous inspection of multiple historical, physical, and diagnostic findings may be formative in determining the anatomical location of the lesion (stomach, small intestine, large intestine, peritoneal cavity), the etiologic category (congenital, nonstrangulating obstruction, strangulating obstruction, inflammatory, or other), or even possibly the specific diagnosis (Table 11-1). In obtaining a history, particular attention should be given to the farm history, use of medications (especially analgesics), risk factors for septicemia or failure of passive transfer, and problems with other foals on the farm.

As some differentials are strictly age-dependent (see Table 11-1), knowing the age of onset of clinical signs is important. In the neonatal period, commonly reported causes of abdominal pain are meconium impaction, small-intestinal volvulus, enteritis or colitis, uroperitoneum, intussusception, gastric ulcers, and ileus secondary to prematurity, septicemia, or neonatal encephalopathy.[4-8] Clinical signs of lethal white syndrome, meconium impaction, and uroperitoneum most commonly manifest in the first 12 to 24 hours, 12 to 96 hours, and 48 to 96 hours of life, respectively. However, if uroperitoneum is the result of urachal or urinary bladder infection, clinical signs may be delayed until 7 to 14 days of age. Although the potential spaces created by congenital or traumatic umbilical, inguinal, and diaphragmatic hernias may be present since birth, incarceration of bowel into these spaces may occur at any age, if at all. Enteritis, colitis, intussusception of small intestine, small-intestinal volvulus, and clinically significant gastric ulcers may develop at any age.

The breed and sex of the foal may provide supportive evidence for certain differential diagnoses. Lethal white syndrome is most commonly reported in all-white to almost-all-white offspring of overo cross overo Paint Horses. In one study of 168 horses with congenital umbilical hernias, the incidence was two times greater in fillies compared to colts, and Thoroughbreds were twice as likely to have an umbilical hernia compared to Standardbreds.[9] In this later study, incarceration of bowel into the umbilical hernia was not reported. Scrotal hernias most commonly occur in Standardbred and Tennessee Walking Horse colts,[8] and fecaliths are frequently reported in American Miniature foals.[6,10] In one study, meconium impactions occurred twice as often in colts compared to fillies.[11] Although the incidence of uroperitoneum is often quoted to occur more commonly in colts, in one recent study, the incidence was approximately equal among the sexes.[12] Additional historic information that should be carefully scrutinized is the general health of the dam, the foal's gestational age, the foaling history and general perinatal health, such as ingestion of colostrum, age at passage of meconium, nursing frequency (see Chapter 1 for review of normal perinatal health), and farm history of potentially infectious causes of enteritis or colitis (Salmonella, rotavirus, Clostridium). Most foals will have passed meconium within 9 to 12 hours of life; however, the gastrocolonic reflex stimulated by ingestion of colostrum frequently initiates earlier passage of meconium. Evacuation of meconium may be delayed (meconium retention) as the result of ileus secondary to another primary non-gastrointestinal disease, such as septicemia or neonatal encephalopathy. In these cases, although passage of meconium may be slower than expected, the delay in passage may not be accompanied by clinical signs of abdominal pain. Passage of "milk feces" or yellow pasty feces does not necessarily indicate that all meconium has been removed from the colon.

CLINICAL SIGNS

Clinical signs of abdominal pain in foals can be highly variable, and the intensity of the signs is not necessarily indicative of the etiology. It is important to note that foals with inflammatory lesions of the intestinal tract or those suffering from general functional ileus secondary to systemic disease can act as violently painful as foals with obstructive or strangulating lesions of bowel. However, in general, foals suffering from uroperitoneum and gastric ulcers have less intense abdominal pain than do foals with inflammatory or obstructive lesions. Repeatedly thrashing or rolling from side to side is generally accepted as a highly representative clinical sign of abdominal pain. However, early signs of abdominal pain in neonatal foals may only manifest as reduced frequency of nursing and prolonged recumbency. Other subtle but significant signs of abdominal pain in foals include general restlessness, especially in recumbency, and/or frequent adjustment of recumbent positions (Figure 11-2). Often recumbent foals with abdominal pain will stretch their limbs, twist their head or neck, roll into dorsal recumbency (Figure 11-3), and make frequent attempts or

Table 11.1 Categorical Differentials for Colic in Foals

Category	Considerations	Common Causes	Less Common Causes
Congenital	Typically manifests signs in the first few days of life Pain without fever	None	**12- to 48-hour Foals** Atresia (ani, coli, recti) Ileocolonic hypogangliosis Chyloperitoneum[37] **Any Age Foal** Hernia (inguinal, scrotal, diaphragmatic) with incarceration Myenteric hypoganglionosis[38]
Obstruction	More commonly present without fever	Meconium impaction (12 to 96 hours old)	Colon displacement or impaction Cecal impaction Small-colon obstruction by polyp or ovarian ligament[7] **Older Foals** Ascarids (four to 24 months)[39] Fecalith in American Miniatures (typically >1 month old) Phytobezoar or Trichophytobezoar Duodenal stricture post ulcers (typically >1 month old) Sand enteropathy Ileal impaction
Strangulation	Intense pain without fever	**Any Age Foal:** Small-intestinal volvulus Intussusception	Large-colon volvulus Incarceration of bowel through mesodiverticular band Small-intestinal volvulus around Meckel's diverticulum or vitelloumbilical band Incarcerated hernia
Inflammatory	Variable pain, often with fever, diarrhea, or clinical evidence of sepsis	Necrotizing enterocolitis *Clostridium perfringens* *Rotavirus* *Salmonella*	*Cryptosporidia* (rare) *Giardia* (very rare) *Aeromonas* NSAIDS Antimicrobial-induced peritonitis Intra-abdominal abscess Adhesions **Older Foals** *Rhodococcus equi* intra-abdominal abscess or colitis *Lawsonia intracellularis* enteritis
Other	Mild to moderate pain without fever; diarrhea may be present with gastric ulcers	Gastric ulcers Uroperitoneum (typically two to seven days old) Functional ileus secondary to septicemia, prematurity, neonatal asphyxia, neonatal encephalopathy, overeating, milk replacer	Ovarian torsion—very rare[8,40] Hemoperitoneum[41]

strain to either defecate and/or urinate. In the standing foal, signs that are classically associated with straining to defecate include frequent tail swishing, a "water spout" tail, and a "camped under" leg stance with a dorsiflexed back (Figure 11-1). In contrast, a flat or ventroflexed back with the hindlimbs stretched backward and the tail held up is associated with urination (Figure 11-4). Other signs of abdominal pain include lip curling, flank biting or watching, pawing at the ground, and kicking at the abdomen. *It is important to recognize that often critically ill foals that are stuporus will not overtly demonstrate classic signs of*

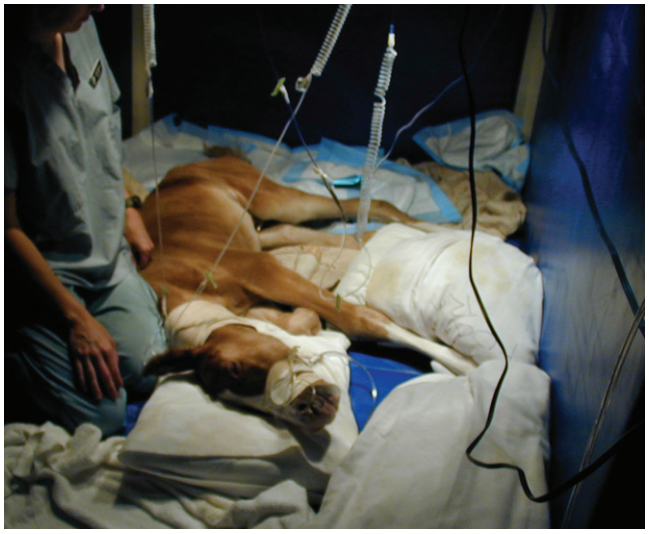

Fig. 11-2 Clinical sign of abdominal pain. There are various clinical signs of abdominal pain in the neonatal foal. This foal has neonatal encephalopathy with secondary intestinal ileus. His abdominal pain was low-grade and manifested by neck twisting, frequent stretching of the forelimbs, and general restlessness.

Fig. 11-3 Clinical signs of abdominal pain. This foal has acute enterocolitis and is demonstrating more classic and intense signs of abdominal pain: recumbency with rolling into a dorsal position and forelimbs retracted up over the neck and head.

abdominal pain, despite the presence of serious gastrointestinal disease.

The colicky neonatal foal should receive a thorough general physical examination with careful attention given to identification of clinical signs or physical evidence of sepsis (see Chapter 5). Sepsis may be directly associated with the primary etiology of the abdominal pain or it may develop secondary to bacterial translocation if the integrity of the gastrointestinal mucosa is compromised. The presence of fever, depression, petechiae, injection, synovitis, uveitis, or diarrhea may be cardinal clues that the abdominal pain has an inflammatory etiology. Although the presence of diarrhea may be an important sign of enterocolitis, intense abdominal pain frequently precedes the onset of diarrhea. Tachycardia and/or tachypnea are expected findings despite etiology. Persistent tachycardia (heart rate >120 beats per minute) has been suggested to be more

Fig. 11-4 Stance to urinate. This foal is demonstrating the typical stance seen with urination: tail straight up, back flat, hind limbs slightly stretched back. Compare this foal's stance to the stance in Figure 11-1.

commonly associated with surgical disorders of the abdomen, compared to medical etiologies.[13] Gross abdominal distension will develop with gas or fluid accumulation in the bowel or abdomen. Severe abdominal distension with intense pain that elicits high-pitched "pings" with percussion is consistent with gas-distended large intestine or cecum. Repeated measurement of the abdominal circumference may be helpful in more objectively determining the course of progression of abdominal distension. Typically, the absence of intestinal sounds is not helpful in determining etiology; however, increased borborygmi may be associated with enteritis or colitis. If diarrhea is present with signs of abdominal pain in a foal, additional fecal diagnostics may be indicated (see Case 11-3).

Unlike mature horses, transabdominal wall palpation can be performed in the neonate and may identify gastric distension, hepatomegaly, thickened or distended bowel, meconium, and the urinary bladder. The ventral abdomen and inguinal rings should be carefully examined for evidence of herniation. Ballottement or succussion of the abdomen may verify a fluid wave compatible with excess fluid in the peritoneal cavity. With adequate restraint or sedation, a careful digital rectal examination may identify meconium or ingesta in the pelvic inlet. A nasogastric tube should be passed in all foals with clinical signs of abdominal pain. Compared to mature horses, successful retrieval of gastrointestinal reflux can be frustrating in the neonate, even in the presence of proximal

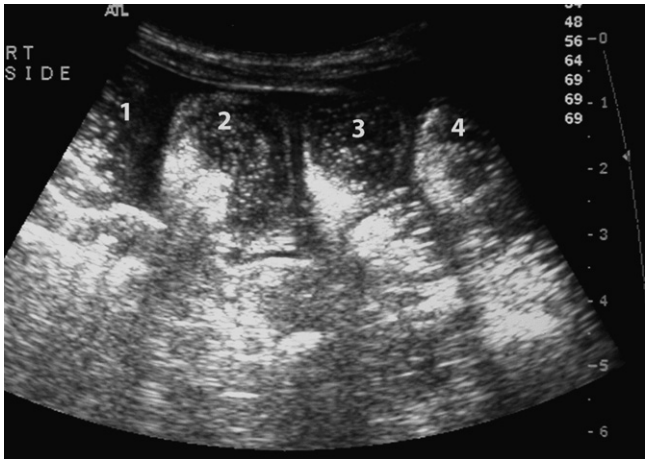

Fig. 11-5 Ultrasonographic image obtained on '03RockN'Roll at 26 hours of age with acute abdominal pain. This image was obtained using a 7-4 MHz curvilinear probe set to a depth of 6 cm. Note the four "balls" of meconium of mixed echogenicity in small colon *(1, 2, 3, 4).* This image was obtained from the left caudoventral abdomen.

intestinal disease. Frequently, nasogastric tubes that are designed for neonatal enteral feeding are of insufficient size for gastric decompression. With this in mind, the largest-bore tube that can be comfortably passed should be used, and persistent attempts should be made to obtain gastric reflux, either by suction or priming the tube with water.

A complete blood count and serum biochemical profile were obtained from '03 RockN'Roll. The PCV was normal at 32%. The total white blood cell count was 9,600/µl, characterized by a normal neutrophil count (6,582/µl) with a significant left shift (864/µl). The only significant abnormalities identified on the serum biochemical profile were hypoproteinemia (total serum protein 3.4 g/dl) with a normal albumin concentration of 2.2 g/dl and hyperglycemia 148 mg/dl. A SNAP test (IDEXX Laboratories, Inc., Westbrook, ME) was performed and confirmed hypogammaglobulinemia with an approximate IgG concentration of 400 to 800 mg/dl.

Blood was obtained for a blood culture, and a 16 g polyurethane catheter was placed in the jugular vein. A transabdominal ultrasound examination was performed using a 7-4 MHz probe and revealed ingesta of variable echogenicity, surrounded by a gas pattern, in several sections of bowel in the left caudal dependent abdomen (Figure 11-5). The diameter of the bowel in this location was approximately 2 cm. There were no other significant findings on the transabdominal ultrasound examination. Based on the history, physical findings, and transabdominal ultrasound examination, meconium impaction was suspected. Based on the presence of a significant left shift and partial failure of passive transfer, the potential for secondary sepsis was increased.

CLINICAL PATHOLOGY

Changes in the leukogram or serum biochemical analysis may provide indirect etiologic evidence. Neutropenia, neutrophilia, a significant left shift, toxic changes within the neutrophils, and hyperfibrinogenemia are indicative of an inflammatory or infectious etiology and if present in the equine neonate, aseptic collection of additional blood for culture is recommended. Hypoglobulinemia is indicative of failure of passive transfer and should be verified by specific IgG testing (see case 3-1). Panhypoproteinemia is indicative of loss and may accompany severe inflammatory lesions of bowel. Azotemia, hyponatremia, hypochloremia, and hyperkalemia may occur with enteritis, colitis, or uroperitoneum. Marked acidosis most commonly occurs in foals with inflammatory lesions of the bowel.

Many clinicians are hesitant to perform an abdominocentesis on a neonatal foal as the risk for complications such as inadvertent enterocentesis or omental prolapse occur more commonly in foals undergoing an abdominocentesis, as compared to adult horses. *Many clinicians perform a transabdominal ultrasound examination first to assess potential risks of performing an abdominocentesis versus the likelihood of successfully obtaining peritoneal fluid.* If an ultrasound examination reveals widespread and/or grossly distended loops of intestine, and/or free peritoneal fluid is difficult to identify, the chances of an uncomplicated and successful abdominocentesis are reduced. An abdominocentesis may be completed on the standing foal or with the foal in lateral recumbency. In either position, proper restraint is imperative and is best facilitated by light sedation (Table 11-2).

The procedure for performing an abdominocentesis in a foal is similar to the adult horse, using either a 20- to 18-gauge 1.5-inch needle or a teat cannula to collect the peritoneal fluid. First, the hair from the ventral midline of the rostral abdomen should be clipped and the skin sterilely prepared. The subcutaneous tissue of the abdominocentesis site in the rostral midline of the abdomen should be infiltrated with 0.5 ml of 2% lidocaine. When a teat cannula is used, entry through the abdominal wall must be preceded by a stab incision made with a number 15 blade through the skin and external portion of the linea alba. Although use of an 18-gauge needle is expeditious, there may be a greater risk of inadvertent enterocentesis or bowel laceration; however, enterocentesis may also occur with a teat cannula if the intestine is grossly distended. Localized or generalized peritonitis may develop subsequent to an enterocentesis, and prophylactic use of parenteral antimicrobials is recommended.

Table 11.2 Analgesics and Sedatives for Abdominal Pain in Foals

Drug	Dosage	Route	Comments
Flunixin meglumine	0.25 mg/kg q 8–24 hours 1.1 mg/kg q 12–24 hours	IV	Avoid repeat dosing
Xylazine hydrochloride	0.1–0.5 mg/kg up to 1 mg/kg	IV IM	Causes GI stasis, bradycardia, hypotension; avoid repeat dosing
Detomidine	10 µg/kg	IV or IM	More potent than xylazine, thus its use is discouraged in neonatal foals
Diazepam	0.05–0.2 mg/kg	IV	For sedation
Butorphanol tartrate	0.01–0.04 mg/kg up to 1 mg/kg	IV IM	May cause excitation or incoordination; frequently combined with xylazine
Pentazocine lactate	0.3–0.4 mg/kg	IV or IM	Less effective than butorphanol
N-butylscopolammonium bromide (Buscopan™)	0.3 mg/kg	Slowly IV	Anticholinergic for spasmodic pain; not label-approved for nursing foals; may cause transient tachycardia; avoid repeat dosing

More commonly, use of a teat cannula results in inadvertent prolapse of omentum through the abdominocentesis site upon collection of peritoneal fluid or removal of the cannula. If this happens, the omentum should be sharply transected with a sterile blade at the abdominal wall and tucked back into the abdominal cavity with another sterile teat cannula.

Normal peritoneal fluid should be light yellow in color and clear. The normal mean nucleated cell count in the peritoneal fluid of healthy foals was reported to be 450 cells/µl (range 60 to 1,400 cells/µl) for 17 foals that were 13 to 134 days of age[14] and 1,400 cell/µl (±1077) for 32 Thoroughbred foals that were 14 to 75 days of age.[15] Both of these reference ranges for nucleated cell counts are lower than means reported for healthy adult horses. The mean protein concentration by biochemical biuret determination and refractive index in foals was reported to be 1.2 g/dl and 1.6 g/dl, respectively.[14] The interpretation of peritoneal fluid nucleated cell count and protein concentration is similar to adult horses with abdominal pain and does not necessarily definitively distinguish etiology or medical from surgical causes of colic. Sanguinous fluid can be present with either severe enterocolitis or strangulating lesions of bowel. Special attention should be given to the cytologic examination. The presence of degenerative neutrophils or bacteria is worrisome (Figure 11-6) and is indicative of loss of the mucosal integrity, bowel rupture, or primary sepsis in the peritoneal cavity. In one study, 78% of colicky foals with peritoneal fluid protein concentrations >2.5 g/dl that subsequently underwent an exploratory laparotomy were euthanized.[8] When uroperitoneum is suspected, the creatinine concentration of both peritoneal fluid and serum should be simultaneously assessed. A peritoneal fluid creatinine to serum creatinine ratio >2 is supportive evidence of uroperitoneum. When determining peritoneal fluid creatinine concentration on an automated chemistry analyzer, it is important to use plasma or serum methodology on the abdominal fluid. If urine methodology is used to determine the creatinine concentration on a peritoneal fluid sample, erroneously increased creatinine concentration may lead to an incorrect diagnosis of uroperitoneum.

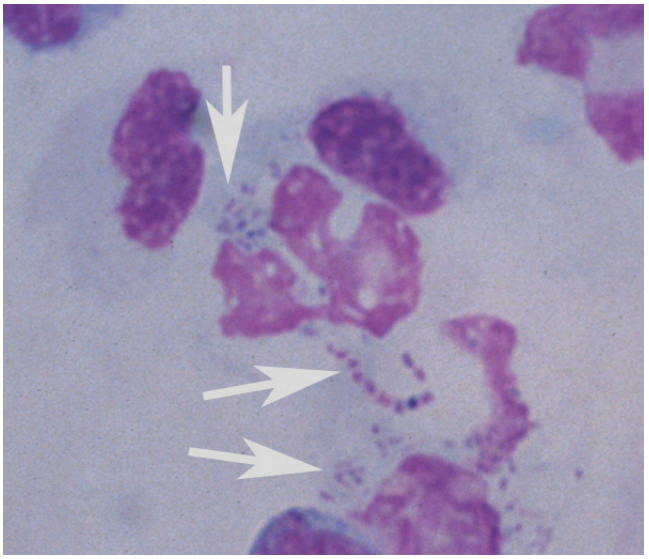

Fig. 11-6 Septic peritoneal fluid cytology. This peritoneal fluid was obtained by abdominocentesis from a 96-hour-old foal with acute abdominal pain and clinical signs of cardiovascular compromise. Note the degenerative neutrophils and the pleomorphic population of bacteria of various-sized rods and a chain of cocci *(arrows).* The mixed population of bacteria is indicative of bacterial translocation across a severely compromised gastrointestinal wall, or gastrointestinal rupture. An exploratory celiotomy confirmed a perforated jejunal intussusception.

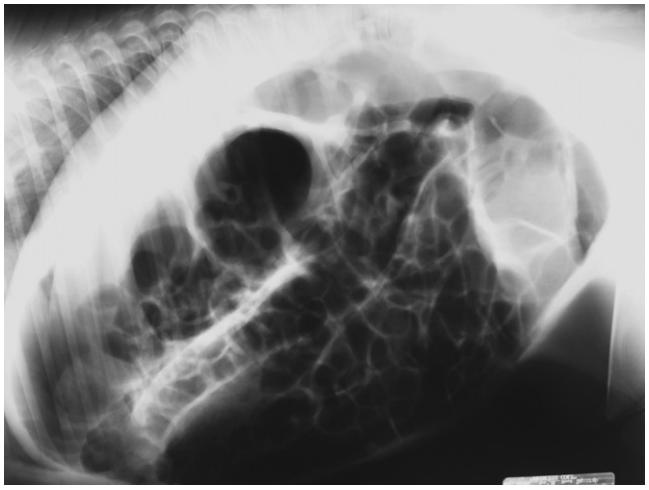

Fig. 11-7 Radiographic appearance of a strangulating obstruction. This abdominal radiograph was obtained from a four-day-old foal and reveals generalized gas distension in both the small and large intestine. A small-intestinal volvulus was identified at surgery.

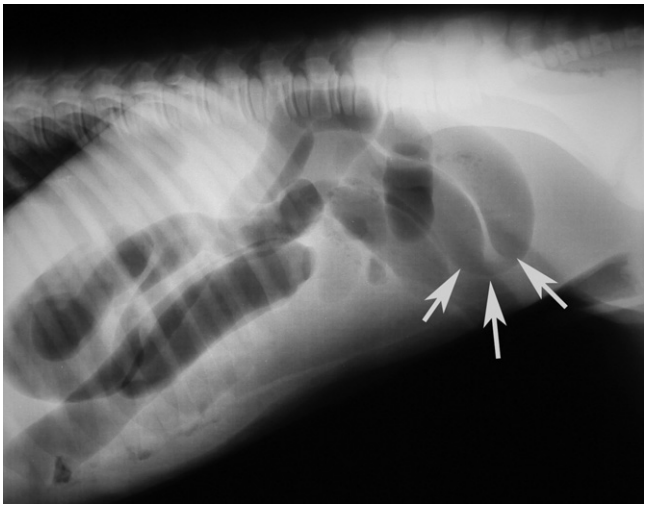

Fig. 11-8 Radiographic appearance of a small-intestinal obstruction. This neonatal foal had radiographic signs of small-intestinal obstruction, as evidenced by isolated loops of gas-distended small intestine that form a *U*-turn or "hairpin" turn *(arrows).* An exploratory celiotomy confirmed a jejunal intussusception.

DIAGNOSTIC IMAGING

Unlike mature horses, abdominal radiography can provide useful information in a colicky neonatal foal. Grid, rare-earth screens and sufficient mAs (5 to 28) and kVp (80 to 120) should be used.[16] Radiographs may be taken with the foal either standing or in lateral recumbency; however, keep in mind that fluid-gas interfaces are easier to detect in the standing foal, when the radiographic beam is horizontal or perpendicular to the dorsoventral plane of the gas/fluid interface in the abdomen. Both right and left lateral views should be obtained as some structures will be more obvious, depending upon which side of the abdomen is closer to the film. Ventrodorsal views may only be possible in small foals or those that are stuporus, sedated, or anesthetized. This view will optimize identification of the pylorus, the descending duodenum, the base of the cecum, the left colon, and the transverse colon.[17] Some degree of gas is normally visible in the stomach, small intestine, cecum, and small colon.

In general, plain film abdominal radiology is more likely to provide information on the anatomic location of the problem than information directly leading to the exact etiology.[8,16,17] For example, gas distension of the small intestine is a nonspecific finding that may occur with enteritis, functional obstruction (ileus), or mechanical obstruction (Figure 11-7). However, if small-intestinal distension is accompanied by "hairpin" or "*U*-shaped" turns of the bowel (Figure 11-8) or multiple, uneven intraluminal gas-fluid interfaces (Figure 11-9), it is more likely associated with mechanical obstruction, though these findings can also

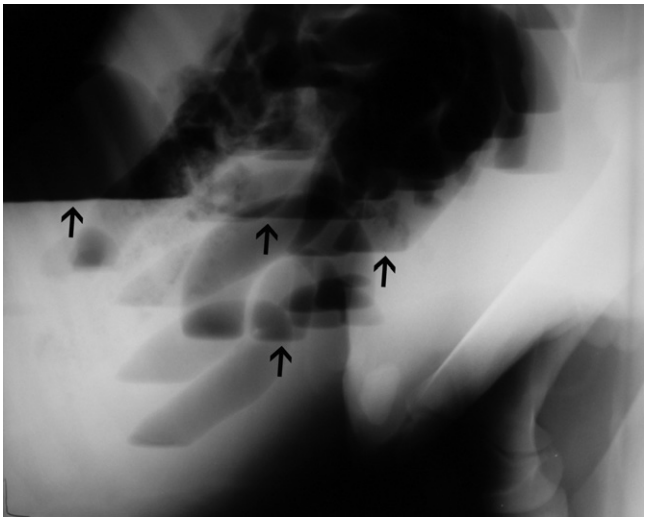

Fig. 11-9 Radiographic appearance of small-intestinal disease. The presence of multiple gas-fluid interfaces at different levels is often considered radiographic evidence of small-intestinal obstruction; however, it can also be seen in foals with intense ileus from enteritis, as was the situation for the foal depicted in this figure.

occur with enteritis or functional ileus. Thickened walls of small intestine may appear uneven or "corrugated" when caused by enteritis (Figure 11-10). Severe generalized gas distension of large intestine is more commonly associated with mechanical obstruction than with inflammatory lesions of large colon (Figure 11-11). Meconium frequently appears as granular contents in the ascending or descending colon (Figure 11-12). Pneumoperitoneum suggestive of bowel

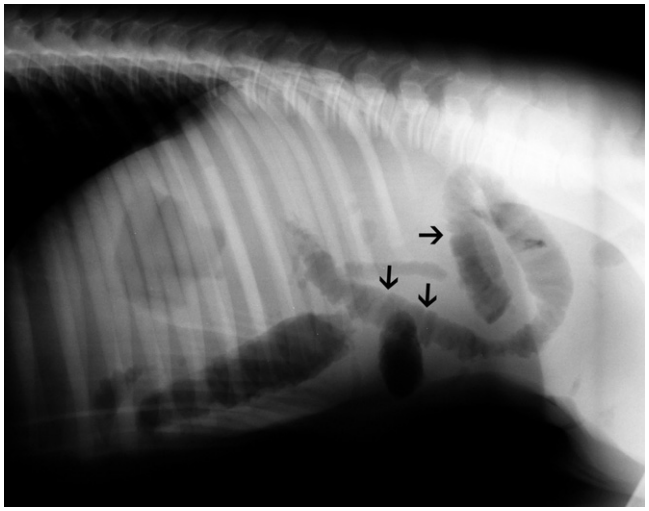

Fig. 11-10 Radiographic appearance of enteritis. Foals with enteritis may have numerous nonspecific radiographic findings, such as gas-distended small intestine and multiple gas-fluid interfaces. In the radiograph depicted here, the finding of individual loops of mildly to moderately gas-distended small intestine with irregular or "corrugated" walls is highly indicative of enteritis.

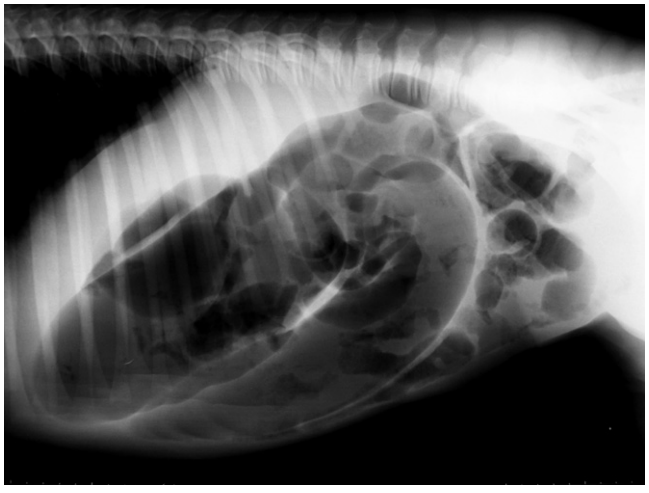

Fig. 11-11 Radiographic appearance of a large- or small-colon obstruction. Unlike small-intestinal gas distension, generalized gas distension of large colon is considered to be fairly specific for large- or small-colon obstruction. This foal had a distal meconium impaction.

rupture should be suspected if there is a gas cap in the dorsal aspect of the abdominal cavity, if the serosal surfaces of bowel are enhanced, or if visualization of the renal silhouettes is improved. Iatrogenic pneumoperitoneum should be considered if an abdominocentesis was performed prior to abdominal radiography.

Finally, abdominal radiography obtained on foals with necrotizing enterocolitis may demonstrate the pathognomonic sign of pneumatosis intestinalis, or intramural air. Radiographic signs of pneumatosis

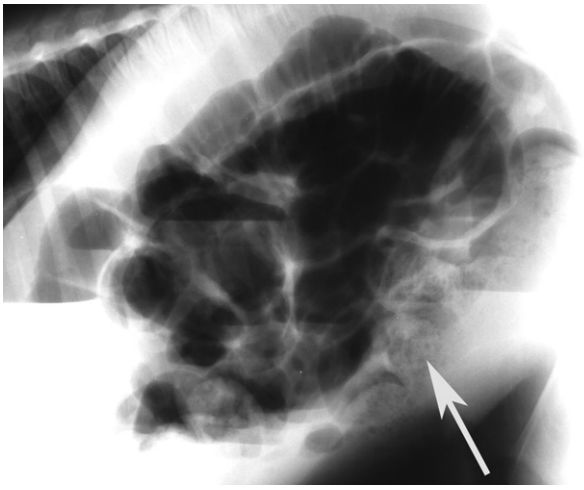

Fig. 11-12 Radiographic appearance of a meconium impaction. In addition to generalized gas distension of the large intestine, neonatal foals with meconium impactions may have radiographic evidence of excessive meconium, which often appears as granular contents within bowel in the ventrocaudal or caudodorsal abdomen *(arrow).*

intestinalis are spectacular and include localized cystic collections that appear as radiolucent "bubbles" in the bowel wall, or diffuse linear strips or flat oval-shaped areas of radiolucency in the bowel wall flanked by the radiopaque serosa and mucosa, when the bowel wall is viewed end-on.[18]

Contrast radiography also has some specific indications in neonatal foals. An upper gastrointestinal contrast study can be used to document delayed gastric emptying of older foals with suspected pyloric outflow obstruction.[16] Foals less than two weeks of age ideally should be fasted for four hours, and foals consuming solid feeds should be fasted for 12 hours prior to contrast radiography.[17] Barium is administered by gravity flow via a nasogastric tube (5 ml/kg as a 30% weight/volume solution), and abdominal radiographs are obtained every 30 minutes. If barium remains in the stomach for longer than two hours, delayed gastric emptying should be suspected but does not necessarily distinguish between mechanical or functional obstruction. Barium should normally reach the cecum and transverse colon by two hours and three hours, respectively, in 10- to 12-day-old foals.[16,17] Barium transit time to the transverse colon is five to eight hours in foals one to two months of age. In addition to documenting transit time, stenosis or abnormal bowel wall may be highlighted by the contrast (Figure 11-13). Lower-intestinal contrast studies (i.e., barium enema) have been reported to have 100% sensitivity and 100% specificity for identifying mechanical obstruction (meconium impaction, atresia coli) of the transverse colon or small colon in foals less than 30 days of age (Figure 11-14).[19] The foal should be restrained or lightly

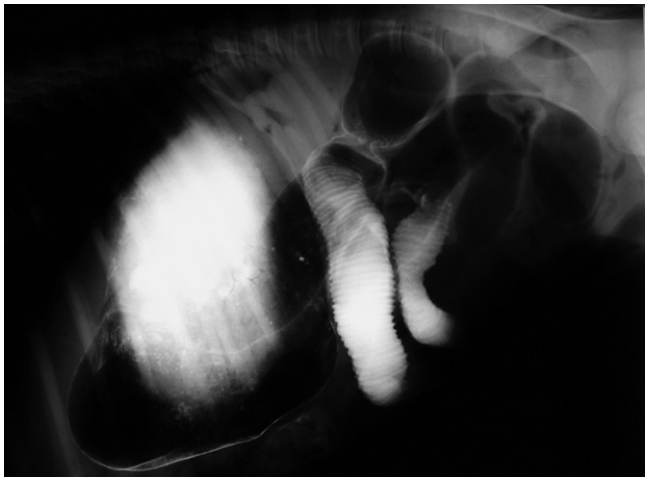

Fig. 11-13 Contrast radiographic evidence of enteritis. This abdominal radiograph was taken approximately 30 minutes after oral administration of barium to a foal with clinical signs of colic. Note the contrast highlighting the distended small intestine with distinctly abnormal loops of corrugated or thickened walls that appear as chains of rings in long axis.

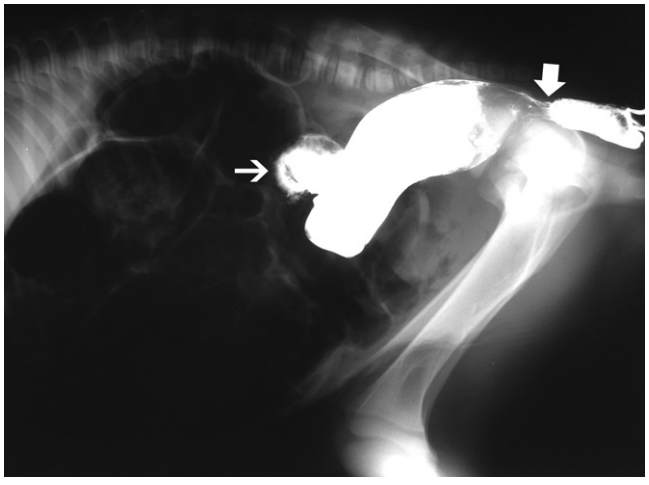

Fig. 11-14 Barium enema demonstrating distal obstruction. Administration of barium as an enema (see text) reportedly has 100% sensitivity and 100% specificity for identification of small or large-colon obstructions. The abrupt end of contrast in the small colon in this foal was highly indicative of atresa coli *(thin arrow)*, which was later confirmed at necropsy. Also note the stenosis of the rectum above the pelvis *(thick arrow).*

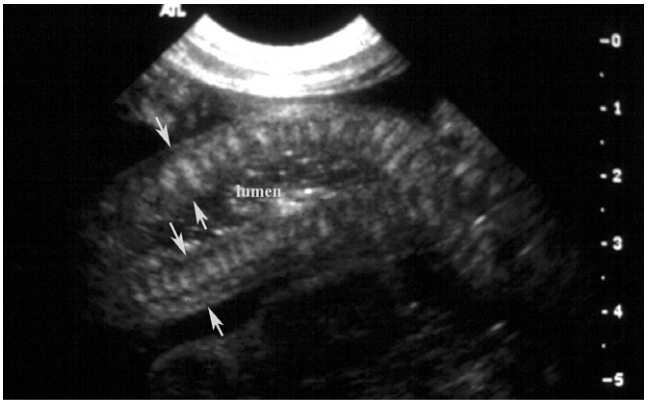

Fig. 11-15 Ultrasonographic appearance of enteritis. This image was obtained with a 7-4 MHz curvilinear probe set to a depth of 5 cm. Note the thickened and irregular wall of small intestine. Normal thickness of the jejunal wall is <4 mm. This foal's small-intestinal wall was almost 1 cm thick *(between arrows).*

sedated and placed in lateral recumbency. A 24-french Foley catheter is placed into the rectum and the bulb gradually inflated. By gravity flow, administer up to 20 ml/kg of 30% weight/volume barium.

Two-dimensional transabdominal ultrasonography is a valuable diagnostic tool in the colicky neonatal foal. Scanning techniques for the foal abdomen are extensively reviewed elsewhere,[20] though a brief review follows here. Standard linear array 4 to 7 MHz transducers are sufficient for visualization of most intra-abdominal structures in the neonatal foal; however a curvilinear transducer will optimize image quality. The foal may be scanned in either lateral recumbency or standing; however keep in mind that fluid-filled, thickened, or enlarged structures may descend to the dependent portion of the abdomen and could be overlooked if only the nondependent side of a recumbent foal is scanned. Furthermore, gas in non-dependent bowel, especially gas in large colon, may preclude examination of deeper structures in laterally recumbent foals. Visualization of intra-abdominal structures is facilitated by clipping the abdominal hair; however thorough wetting of the hair with water or alcohol, in addition to acoustic coupling gel, may be sufficient. In the colicky neonate, transabdominal ultrasonography can be used to identify fluid-distended structures (i.e. stomach, small intestine, large intestine, urinary bladder), gastric or intestinal wall thickness, abnormal intestinal contents (i.e. meconium, fecaliths, phytobezoars, or trichophytobezoars), peritoneal fluid, and to determine intestinal motility.

Normal gastric wall thickness in foals should be less than 7 mm, whereas intestinal wall thickness is 3 to 4 mm. Foals with gastritis or gastric ulcers may have a thickened or irregular gastric wall. Likewise, foals with enteritis or colitis will frequently have diffusely increased small and/or large intestine wall thickness (Figure 11-15). This feature alone does not definitively identify enteritis, as edematous bowel that develops as the result of strangulation (volvulus or intussusception) will also appear regionally thickened (Figure 11-16), with distended fluid-filled intestine proximally. The presence of gas echoes in the intestinal wall, a thickened hypoechoic wall that appears "wavy," or the presence of sloughed mucosa in the lumen are more consistent with a diagnosis of enteritis and should be

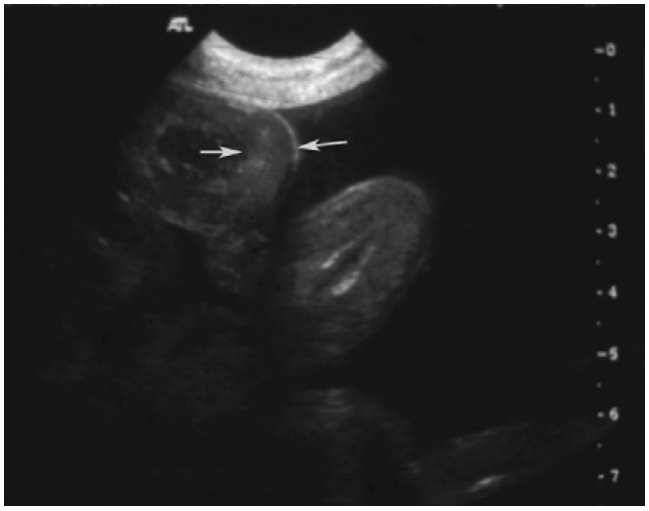

Fig. 11-16 Ultrasonographic appearance of edematous small intestine. This image was obtained with a 7-4 MHz curvilinear probe set to a depth of approximately 7 cm. Note the excessive anechoic peritoneal fluid that surrounds the small intestine with an approximate wall thickness of 1 cm *(between arrows).* This foal had a small-intestinal volvulus.

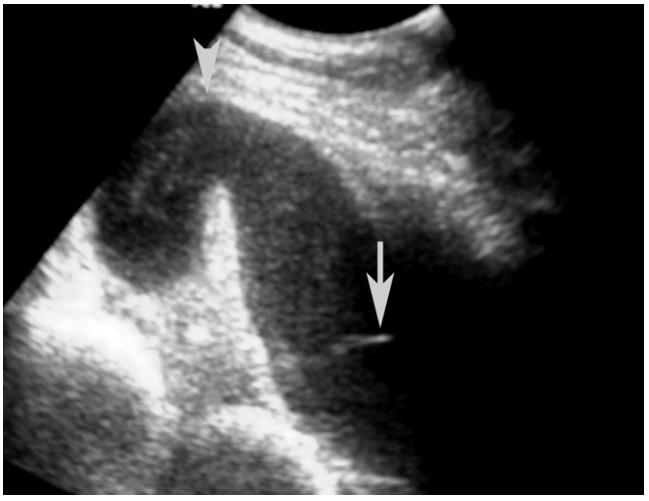

Fig. 11-18 Ultrasonographic appearance of small-intestinal obstruction. This image was obtained with a 7-4 MHz curvilinear probe set to a depth of 8 cm. Note the *U*-turn or hairpin turn in the fluid-distended small intestine *(arrowhead).* This foal had an ascarid impaction that was confirmed with an exploratory celiotomy. Note the ascarids in the lumen of the distended small intestine *(arrow).*

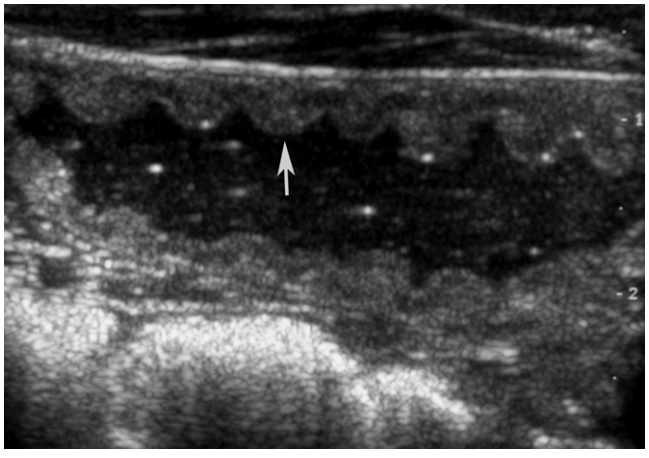

Fig. 11-17 Ultrasonographic appearance of enteritis. This image was obtained with a 7-4 MHz linear array probe set to a depth of approximately 3 cm. The wavy edge of the small-intestinal mucosa *(arrow)* in this long-axis view of fluid-distended small intestine is a finding that is most frequently detected in foals with enteritis.

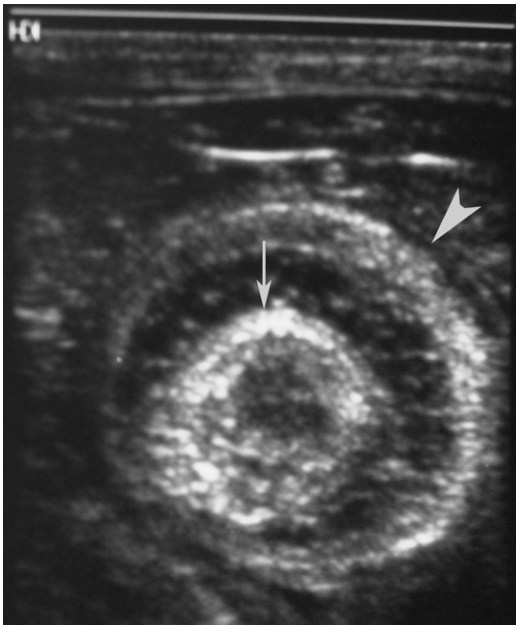

Fig. 11-19 Ultrasonographic appearance of an intussusception. This image was obtained with a 7-4 MHz linear array probe set to a depth of 4 cm. The "target" or "bull's-eye" appearance of concentric rings is created by the thickened and distended outer loop of small intestine *(arrowhead)* separated by fluid from the thickened entering loop of small intestine *(intussusception, arrow)*, as viewed in short axis.

considered as distinguishing features from strangulating lesions (Figure 11-17). Foals with enteritis or colitis may demonstrate either hypermotile or hypomotile bowel, whereas functional ileus and mechanically obstructed intestine more often will appear hypomotile. Neonatal foals with mechanical obstruction of small intestine may have hairpin or *U*-shaped turns of the small intestine when viewed in long axis (Figure 11-18). The unique regional presence of a double intestinal wall or what appears to look like a "bull's-eye" of multiple concentric rings in a short axis view of small intestine is consistent with an intussusception (Figure 11-19), which most commonly is seen in the dependent portion of the abdomen.

Meconium may appear hyperechoic, hypoechoic, or as a mixture of echogenicities in hypomotile intestine.

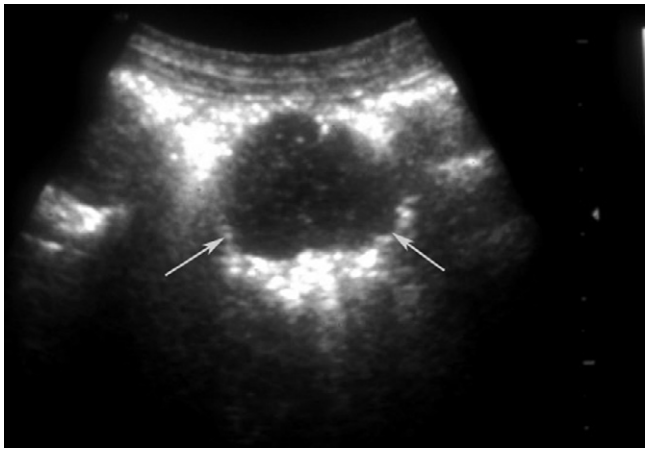

Fig. 11-20 Ultrasonographic appearance of meconium. This image was obtained with a 7-4 MHz curvilinear probe set to a depth of 6 cm and shows a single "ball" of fairly uniformly hypoechoic meconium *(arrow)*, surrounding by gas in the small colon.

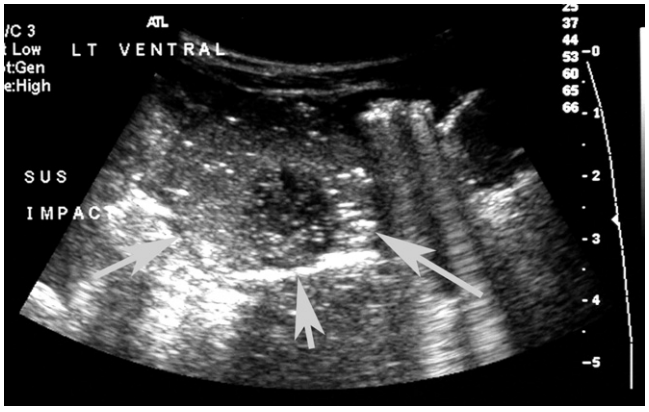

Fig. 11-21 Ultrasonographic appearance of meconium. This image was obtained with a 7-4 MHz curvilinear probe set to a depth of 5 cm and shows a single "ball" of meconium *(arrows)* with mixed echogenicity in the small colon.

Fluid- or gas-distended intestine may be present proximal to the obstruction (Figures 11-20 and 11-21). When present in the small colon, retained or impacted meconium often appears as a row of "balls" and is most easily identified in the dependent portion of the left caudal abdomen in the standing foal. It may be traceable dorsal to the urinary bladder and often is surrounded by a thin layer of hyperechoic gas in sacculated intestine (small colon). Meconium in large colon typically is more amorphous. Extensive gas in the large colon frequently hinders visualization of other intra-abdominal structures and can be associated with mechanical obstruction, though it may also occur with acute colitis. The sonographic appearance of abdominal abscesses is variable, but in the neonatal foal, intra-abdominal abscesses are often associated

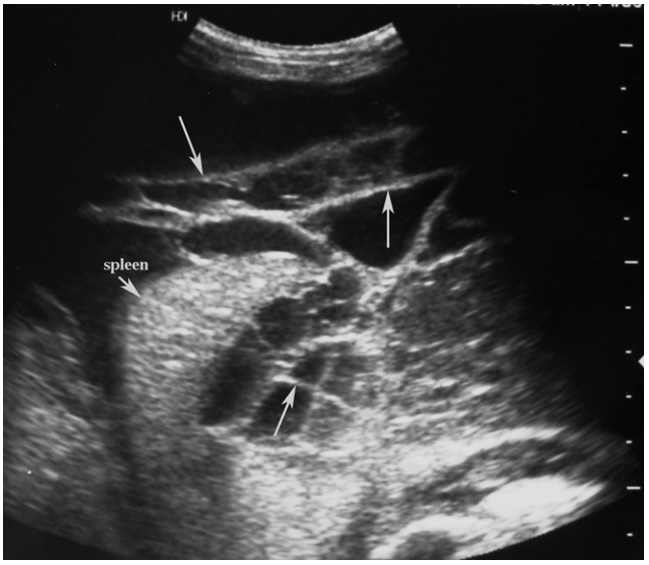

Fig. 11-22 Ultrasonographic appearance of intra-abdominal adhesions. This image was obtained with a 7-4 MHz curvilinear probe set to a depth of 11 cm. This foal developed septic peritonitis as a sequela to severe necrotizing enterocolitis. Note the excessive amount of peritoneal fluid containing numerous fibrin strands *(arrows)*, connecting loops of bowel, and the spleen. This foal was euthanized due to recurring bouts of abdominal pain, despite resolution of the enteritis.

with umbilical remnants, previously devitalized bowel, or mesenteric lymph nodes. Finally, the presence of excessive anechoic fluid may be indicative of uroperitoneum (see Chapter 12), though anechoic transudate may also develop as a result of enteritis, colitis, or strangulation. Hyperechoic densities within peritoneal fluid may represent fibrin strands, leukocytes, or adhesions (Figure 11-22). The presence of gas echoes free within the peritoneal fluid is indicative of a ruptured viscus.

Gastroscopy may be accomplished with a 1-meter endoscope in a neonatal foal and is covered elsewhere in more detail later in this chapter (see Case 11-2). For most neonatal foals, suckling can be allowed prior to gastroscopy, but solid-feed consumption should be withheld for 6 to 10 hours.[21] Caution should be exercised in the interpretation of the clinical significance of gastric ulcers in foals, as up to 50% of young asymptomatic foals have gastric ulcers along the margo plicatus of the greater curvature of the stomach, and gastric ulcers may develop secondary to another primary gastrointestinal disorder.[22,23] However, multiple deeper ulcers, bleeding ulcers, ulcers along the lesser curvature or in the glandular mucosa, or those accompanied by clinical signs that are consistent with gastric ulceration should be considered clinically significant.

DIFFERENTIAL DIAGNOSIS

Most information on colic in the neonate is obtained from referral institutions or, more often, from foals undergoing exploratory celiotomy for acute abdominal pain; therefore the data may not precisely reflect the true incidence of each reported etiology. The only published study on 20 foals less than two weeks of age with acute abdominal pain reported that an exploratory celiotomy revealed functional ileus (45%), meconium impaction (25%), large-colon displacement (15%), small intestine displaced around the base of the cecum (10%), ruptured gastric ulcer, and small colon obstructed by the ovarian ligament.[7] Other retrospective studies of abdominal surgery in the foal include foals three to six months of age and thus it was difficult to ascertain the etiology of abdominal pain exclusive to the neonatal period. In 53 foals that underwent an exploratory celiotomy from birth to three months of age, meconium impaction, uroperitoneum, enteritis, small-intestinal strangulation (herniation with incarceration, small-intestinal volvulus, and intussusception), and enteritis accounted for 80% of the total cases.[4] In a study that reviewed 83 foals up to six months of age, the most commonly reported diseases identified at surgery were small-intestinal volvulus, meconium impaction, and intussusception.[8] These reports underscore the difficulty in definitively identifying the cause of abdominal pain prior to exploratory celiotomy in neonatal foals, as clearly some of these cases, such as enteritis and functional ileus, would not be considered to be predominantly surgical diseases. *Furthermore, it is noteworthy that if the etiology of the abdominal pain cannot be ascertained in the violently painful patient, an exploratory celiotomy may be indicated solely as a diagnostic tool.* The purpose of this section is to provide a brief review of the conditions most commonly reported in the neonatal foal. Table 11-1 provides a more comprehensive list of reported causes of acute abdominal pain in the young foal.

Meconium Impaction

Meconium is the sticky caramelized feces of the newborn foal that comprises intestinal secretions, swallowed amniotic fluid, and cellular debris. In one study of 30 newborn foals, it was reported that the total weight of meconium is equal to 1% of the foal's body weight.[24] Most foals will start to evacuate meconium shortly after the first ingestion of colostrum, which acts both as a laxative and stimulator of the gastrocolonic reflex. The majority of the meconium is evacuated within the first 12 hours of birth and is replaced by "milk" feces, which are pasty and yellow in appearance. However, concurrent disease such as neonatal asphyxia, prematurity, septicemia, and encephalopathy may delay passage. Meconium impaction implies failure to evacuate sufficient quantities of meconium with subsequent development of signs of colonic obstruction: pain, straining to defecate, and abdominal distension secondary to accumulation of gas in bowel proximal to the impacted meconium.

It has been suggested that meconium impaction is more likely to occur in colts[11] and in foals greater than 340 days of gestational age.[25] To the author's knowledge, prophylactic use of an enema at birth has not been shown to prevent meconium retention or impaction. Foals with meconium impaction are disinterested in nursing, strain to defecate, and typically stand with a slightly arched back and frequently "swish" their tail (Figure 11-1). Digital examination may detect meconium within the rectum. Colic, abdominal distension, tachypnea, general restlessness, and tachycardia are frequently reported clinical signs.[11] Intestinal borborygmi are usually present[11] and are not a reliable sign of obstruction. Meconium can usually be identified by either plain or contrast abdominal radiography or ultrasonography (see "Diagnostic Approach to Colic in Neonatal Foals" section above). In more severe obstructions, excessive amounts of gas may accumulate in the large colon, proximal to the obstruction. Rupture of the urinary bladder may occur in foals that strain excessively from meconium impaction.[11] Furthermore, extensive mural damage lends to bacterial translocation and secondary septicemia.

Lethal White Syndrome

Other causes of acute abdominal pain that closely mimic meconium impaction and primarily manifest during the first 24 to 48 hours of life are the rarely reported cases of ileocolonic aganglionosis, atresia coli, and atresia recti. Ileocolonic aganglionosis, or "lethal white" syndrome, is a fatal autosomal recessive disorder principally of overo cross overo Paint Horses that is caused by a point mutation in amino acid 118 in endothelin receptor B.[26] The endothelin receptor is critical for the proper development and migration of cells from the neural crest that ultimately form melanocytes in the skin as well as neurons in the intestinal tract. Thus, foals that are homozygous for the mutation are essentially all white (though some small areas of pigmentation can occur) and develop signs of functional ileus in the first few hours of life (Figure 11-23). Color patterns in the dam and sire that have the highest incidence of heterozygote carriers of the mutation are

Fig. 11-23 Lethal white syndrome. This all-white foal born to an overo Paint mare that was bred to an overo Paint stallion was diagnosed with ileocolonic aganglionosis at necropsy. The defect is caused by an autosomal recessive point mutation in the endothelin B receptor.

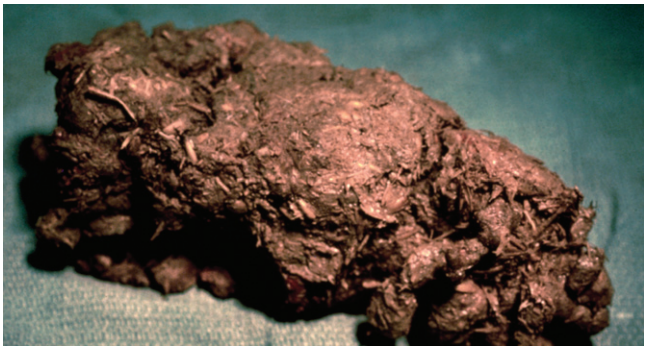

Fig. 11-24 Fecalith. This fecalith was removed by small colon enterotomy from a four-week-old American Miniature foal with acute abdominal pain and gross abdominal distension.

frame overo, highly white calico overo, and frame blend overo horses.[26] However, the heterozygote mutation has been occasionally rarely detected in other white-patterned Paints and "nonPaint" white-patterned bloodlines. It has not been detected in solid-colored breeding-stock Paint Horses without white, but heterozygote adult solid-colored Miniature Horses of Paint lineage and white-patterned horses of breeds other than the Paint Horse have been rarely identified.[26]

Lethal white foals typically are born "normal" in appearance and behavior, with the exception of the mostly white coat. Clinical signs of abdominal pain usually develop in the first few hours of life, after ingestion of colostrum, and progressively develop gross abdominal distension. Evidence of passage of meconium is often missing, though some meconium may be passed. The only way to definitively identify a lethal white foal is by DNA testing for the mutation or histopathologic demonstration of insufficient intestinal ganglia. Unfortunately, it can take weeks to obtain the results of DNA testing and hours to days to obtain the results of intestinal biopsies. Diagnosis is often initially presumptive, based on signalment, heterozygote parents, lack of response to symptomatic treatment, and rule out of other causes by additional diagnostics or surgical exploratory. Affected foals and heterozygote adults can be identified by submitting plucked hair with intact root bulbs from the mane (preferred sample) to the Veterinary Genetics Laboratory at the University of California, Davis, available at www.vgl.ucdavis.edu/service/horse/coatcolor.html. It should be noted that not all white foals of Paint lineage are lethal whites and when tested, these unaffected, rare, all-white Paint Horses are not homozygous for the mutation.

Other Differentials

Atresia coli, recti, or ani are rarely reported causes of colic in the newborn foal that may mimic meconium impaction, based on age of onset and signs of obstructive disease.[27] It may be possible to identify atresia recti on visual or digital examination of the rectum or by protoscopy. Retrograde contrast barium enema usually identifies an abrupt obstruction (see Figure 11-14), but definitive identification may require an exploratory celiotomy. Successful surgical repair has been described; however, other congenital abnormalities have been simultaneously reported and should be ruled out prior to consideration of surgery. The heritability of these defects is not fully known.[27]

Fecaliths are hard concretions of ingesta (Figure 11-24) that may also contain undigested material, such as hair. They most commonly occur in the American Miniature breed and have been reported in foals as young as 19 days of age.[6,10] Affected foals typically present with progressive unresponsive abdominal pain that is accompanied by gross abdominal distension. As fecaliths obstruct the small colon or rectal lumen, abdominal radiographs typically demonstrate gas distension of the large colon. Successful treatment almost inevitably involves a celiotomy with a small colon enterotomy.

Strangulating lesions of the small intestine that require surgery occur more frequently in neonatal foals, as compared to strangulating lesions of the large intestine. Volvulus of the small intestine is the most commonly reported strangulating lesion in foals less than three months of age.[8] Factors leading to development of

these lesions are undetermined, but alterations in motility may contribute. Intussusceptions are most commonly reported in three- to five-week-old foals[2] and may be acute or chronic and intermittent. Small-intestinal intussusceptions are most frequent, but ileocecal and cecocolic intussusceptions have been reported in young foals.[28] Most inguinal and umbilical hernias in foals resolve spontaneously without incarceration of intestine.[8,29-32] In a large retrospective study of 147 foals with umbilical hernias, only 13 required surgical repair.[29] Only 4 of the 13 foals that needed surgery had incarcerated bowel in the umbilical hernia. Although the hernias were present since birth, and strangulation may rarely occur shortly after birth, the majority of foals with strangulating umbilical hernias were not neonates, but most often, affected foals were presented in the first six months of life.[31] The most common presenting complaint in foals with an umbilical hernia with incarcerated bowel was an acute firm enlargement of the hernia that was sensitive upon palpation. Only 30% of foals with strangulated umbilical hernias presented with signs of abdominal pain.

In separate retrospective reports, inguinal hernias in neonatal foals that resulted in incarceration of small intestine that required surgical correction were exclusively found in newborn foals as a result of rents in the vaginal tunic (direct inguinal hernia).[30,32] Onset of clinical signs was typically within 48 hours of birth. Diagnosis should be suspected by the presence of an irreducible mass in the scrotal sac, edema in the scrotum and prepuce, and colic. Diagnosis of either an umbilical or scrotal hernia with incarceration can usually be confirmed by palpation and ultrasonography. It has been suggested that elective herniorrhagy should be considered if an umbilical hernia has been present in foals greater than six months of age or if the defect is larger than 10 cm.[31]

Diaphragmatic hernias are rare in foals and can result from failure of fusion of its embryonic components or from traumatic rupture of the diaphragm *in utero,* at birth, or after birth.[33] Affected foals can remain asymptomatic for prolonged periods of time, but the presenting complaint typically is acute abdominal pain. The intensity and onset of clinical signs is related to the amount of intestine that has herniated into the thoracic cavity and whether the herniated bowel is simply displaced or strangulated.[33] In addition to abdominal pain, tachypnea and/or dyspnea may be present. The diagnosis can be confirmed by either radiographic or ultrasonographic evidence of an incongruous diaphragmatic line, the presence of gas-fluid interfaces indicative of intestine in the thoracic cavity, and/or pleural effusion.

Enterocolitis, gastric ulceration, and uroperitoneum are commonly reported causes of abdominal pain in the neonate and are described separately later in this chapter and in Chapter 12. Functional ileus secondary to prematurity, sepsis, neonatal asphyxia, neonatal encephalopathy, electrolyte abnormalities, concurrent gastrointestinal disease, hypoxic or ischemia bowel, overfeeding, use of milk replacer, botulism, and many other concurrent diseases may induce significant abdominal pain in the neonatal foal. If these underlying conditions are present, careful consideration to additional diagnostics should be used to rule out more serious gastrointestinal disorders (see "Diagnostic Approach to Colic in Neonatal Foals" section above). Simple solutions, such as reducing or eliminating enteral feeding, changing the source of milk, or correction of electrolyte derangements and other underlying disorders should be tried first. However, it may be necessary to consider an exploratory celiotomy for definitive diagnosis and for therapeutic decompression of bowel before initiation of prokinetic therapy. Cecal impaction, large-colon volvulus, large-colon displacement, intestinal infarction, and ileal impaction are considered to be rare disorders of the neonatal foal.

For the suspected meconium impaction, 120 ml of mineral oil was given '03 RockN'Roll via a nasogastric tube. Lactated Ringer's solution was given at a rate of 100 ml/kg/day, as a continuous rate infusion. The foal was given 1 mg of butorphanol and 10 mg of diazepam intravenously. A 4% acetylcysteine retention enema was administered; 40 ml of 20% acetylcysteine was mixed with 160 ml of water. A 30-french Foley catheter was inserted into the anus, and the cuff was slowly inflated to prevent extraction. The acetylcysteine solution was given by gravity flow. After 45 minutes, the cuff was deflated and the Foley catheter was removed. Abdominal distension was monitored by periodically measuring the abdominal diameter using a tape measure. The foal was not allowed to nurse the mare and was continually observed by technical nursing staff.

To address the increased risk of sepsis, 1 liter of plasma was given intravenously and the foal was started on K penicillin (22,000 units/kg IV q 6 hours) and amikacin (21 mg/kg IV q 24 hours). Four hours after presentation, the blood glucose concentration decreased to 80 mg/dl and thus the LRS was supplemented with 2.5% glucose. The foal remained quiet and alert for the next several hours and was intermittently observed to strain. A small amount of meconium was passed six hours after admission. Approximately 10 hours after admission, the foal was observed to roll into dorsal recumbency. An abdominocentesis was performed using an 18-gauge needle. The peritoneal fluid was light yellow in color and had a nucleated cell count of 5,900/µl and a protein concentration of 2.6 g/dl. Cytologic examination revealed 95% nondegenerative neutrophils with occasional Dohle bodies, and 5% mononuclear cells. Microbes were not observed. The foal's TPR remained within normal limits

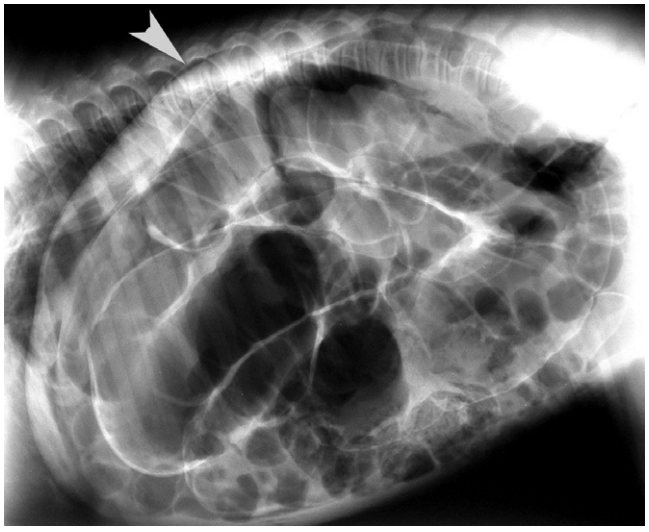

Fig. 11-25 Radiographs obtained from '03 RockN'Roll. These abdominal radiographs demonstrate diffuse gas-distended large intestine, with granular-appearing luminal contents in the caudoventral abdomen. The small amount of free gas visible ventral to the diaphragm *(arrowhead)* and the generalized increased radiopacity of the serosal surfaces are radiographic evidence of pneumoperitoneum.

until 12 hours after presentation, when the rectal temperature was 100.5°F, the heart rate was 176 beats/minute, and respiration was 24 breaths/minute.

A digital rectal examination revealed continued presence of ingesta at the pelvic inlet. Abdominal radiographs were obtained (Figure 11-25) and demonstrated generalized gas distension in the large colon with granular-appearing contents in the lumen. The serosal margin detail was increased, and free gas was noted in the peritoneal cavity. The radiographic findings were consistent with obstruction of the large colon with pneumoperitoneum. The tachycardia and radiographic findings prompted the decision to perform an exploratory celiotomy. An extensive and firm meconium impaction was confirmed in the small colon. Despite aggressive attempts to dislodge the impaction by injection of the impaction with carboxymethylcellulose, accompanied by external mural massage of the small colon, a small colon enterotomy was necessary to remove the impaction. Upon further exploration of the peritoneal cavity, a small full-thickness tear of the transverse colon wall was identified with focal adjacent fecal contamination. With this revelation, the foal was euthanized under anesthesia. A necropsy examination was not performed.

TREATMENT

Medical therapy for meconium impaction includes judicious use of analgesics, intravenous polyionic isotonic fluids, oral laxative therapy, and enemas. Foals with meconium impactions are expected to exhibit some degree of pain. Judicious use of analgesics (Table 11-2) is required to balance the necessity to provide relief from pain and the ability to appropriately assess the patient's progress. Mineral oil (4 to 8 ounces administered via a nasogastric tube) is used for its lubricating effect. Milk of magnesia (1 to 2 ounces) provides an osmotic laxative effect, but should be used sparingly as it may be dehydrating. The detergent dioctyl sodium sulfosuccinate can be quite irritating, and it should be avoided in both oral and rectal therapy.[8] Castor oil therapy has been described,[34] but can provoke violent abdominal pain in the foal.

Enemas are a mainstay of treatment for small-colon meconium impactions. Warm-water liquid detergent (i.e., Palmolive®) enemas (½ teaspoon liquid detergent to 500 ml water) are purportedly gentle to the rectal mucosa and effective. Commercial phosphate enemas (i.e., Fleet®) can also be used, but repeated administration may increase the risk of phosphate toxicity. Recently, acetylcysteine retention enemas have been reported to be a highly successful treatment for meconium impactions in foals.[11] It is hypothesized that the acetylcysteine cleaves disulphide bonds in the mucoprotein molecules in meconium, decreasing its overall tenacity.

A 4% acetylcysteine solution, pH 7.6, is made by adding 20 g of baking soda and 8 g of acetylcysteine to 200 ml of water. A 30-french Foley catheter with a 30 ml bulb is inserted approximately 2.5 to 5 cm into the rectum and, the bulb is slowly inflated to occlude the rectum. One hundred to 200 ml of the 4% acetylcysteine solution is administered by gravity flow and retained for 30 to 45 minutes. The acetylcysteine retention enema was effective in eliminating 78% of meconium impactions within 12 hours.[11] If needed, the acetylcysteine therapy can be repeated in 12 hours, and was repeated up to three times in some cases before resolution of the impaction. Occasionally, repeated use of an enema generates significant rectal and small colon mucosal irritation that sustains signs of straining despite effective removal of the impaction. This continued straining may confound determination of successful treatment.

Surgical intervention should be considered if medical therapy is unsuccessful.[35,36]

When to Consider Surgery

Although there often is no single criterion that distinguishes the course of treatment in any particular case, an exploratory celiotomy should be considered in a foal with abdominal pain (of any etiology) if there is:

- Persistent pain that is unresponsive to analgesics
- Persistent tachycardia, especially a sustained heart rate greater than 120 beats/minute
- Progressive abdominal enlargement
- Increased peritoneal fluid protein concentration and/or nucleated cell count
- Sanguinous peritoneal fluid
- Evidence of sepsis in the peritoneal fluid, without known origin
- Radiographic or ultrasonographic evidence of obstruction
- Deterioration in the foal's condition with a definitive diagnosis not determined
- An owner that is well-informed of the cost and prognosis

OUTCOME

The prognosis for foals with a meconium impaction is generally considered good to excellent with short-term survival reported to be 100%[11] and long-term survival, following either medical or surgical treatment, reported to be 80% to 94%.[35,36] Most meconium impactions will resolve with medical intervention. At the University of California, Davis, from 1987 to 2002, 41 out of 44 foals (93%) with meconium impactions were successfully treated medically with acetylcysteine enemas.[11] About 40% of these former cases required more than one acetylcysteine enema, and in about 20% of cases it took more than 12 hours for the impaction to resolve. Once hospitalized, '03 RockN'Roll received one acetylcysteine enema and oral laxative and intravenous fluid therapy over 12 hours. Prior to surgery, the foal exhibited only mild to moderate signs of intermittent pain (straining to defecate with recumbency and rare dorsal recumbency) and his abdominal size did not significantly increase. The discovery of pneumoperitoneum before celiotomy was worrisome. However, because an abdominocentesis had been performed several hours prior to taking the abdominal radiograph, it was speculated that the pneumoperitoneum was iatrogenic from introduction of room air through the abdominocentesis needle into the peritoneal cavity. The subsequent detection of a ruptured transverse colon during surgery was an unexpected complication. Spontaneous rupture of the colon as a sequela to meconium impaction must indeed be rare, as there are no reports of its occurrence in the American literature. It remains unclear as to when the colon rupture occurred.

At presentation, the foal did not exhibit clinical signs of sepsis, though a small but significant left shift was present on the leukogram. This may have been a result of early sepsis from an unrelated cause or may have been the result of bacterial translocation across compromised mucosa along the colonic impaction. The foal did not exhibit intense signs of abdominal pain, in fact, he only showed signs of straining to defecate during the first 10 hours of hospitalization. Although he received an analgesic dose of flunixin meglumine prior to referral, he only received one other short-acting analgesic prior to surgery: 1 mg of butorphanol. The abdominocentesis was performed at approximately 10 hours of hospitalization, after the foal was observed to roll into dorsal recumbency. Although the nucleated cell count and protein concentration were both increased, there were no signs of sepsis cytologically. Either rupture had not yet occurred or it had already occurred and the peritoneal fluid sample obtained by abdominocentesis was not representative. In retrospect, the pneumoperitoneum seen radiographically at 12 hours of hospitalization most likely was indicative of a localized rupture. The decision to perform an exploratory celiotomy was based upon the lack of passage of a significant amount of meconium, the presence of extensive amounts of meconium in the colon (as seen ultrasonographically and radiographically), the presence of free air in the peritoneal cavity on abdominal radiographs, and the development of persistent tachycardia, with a sustained heart rate greater than 120 beats/minute.

Although the majority of foals with meconium impactions are treated medically, surgery is indicated in some cases. Postoperative intra-abdominal adhesion formation is the most common anticipated complication, thus surgery is often delayed for fear of poor long-term survival. Two short-term survival (i.e., survival until discharge) studies on foals undergoing exploratory celiotomy for meconium impactions had a combined survival rate of 90% (9 out of 10 foals).[4,6] Long-term survival to maturity was 67% (4 out of 6) for foals undergoing surgery with either enterotomy or manual reduction.[36] In a 2002 retrospective study in Germany on 42 foals undergoing an enterotomy for a meconium impaction, long-term survival to six months was 60%.[35] In general, for foals undergoing an exploratory celiotomy, the survival rate is better for foals with lesions of the large colon, compared to the small intestine.[8] Although studies before 1994 indicate that survival rate for foals undergoing surgery for colic is lowest for neonates, data from the early 1990s showed significantly higher survival rates, as compared to the 1980s.[4-6] With advancements in diagnostics and critical care, assuredly the long-term survival has continued to improve, though specific data is unavailable for recent years.

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Case 11-2 Gastric Ulcers and Esophageal Reflux (Endoscopy) Gary Magdesian

Fig. 11-26 '04 Belly Dancer, a three-day-old foal, in dorsal recumbency with signs of abdominal pain.

'04 Belly Dancer, a three-day-old Quarter Horse filly, presented at the clinic for weakness, lethargy, and anorexia. Gestational history was unremarkable. The foal had congenital flexural deformity of the carpi, and had been treated with tetracycline (44 mg/kg, IV) for the contracture. She had been recumbent since birth, and had been assisted to stand to nurse or bottle feed in sternal recumbency. However, the foal had refused milk in the last 18 hours and she frequently assumed a dorsal recumbent position (Figure 11-26). On presentation the foal was in hypovolemic shock, as evidenced by tachycardia (166 beats/minute), cold extremities, weak peripheral pulse quality, and tacky mucous membranes. The foal was estimated to be 10% dehydrated. The carpi demonstrated mild contracture bilaterally.

After rehydration with lactated Ringer's and dextrose (2.5%), the foal's heart rate decreased and mentation improved. Upon increasing arousal, bruxism and ptyalism became apparent (Figure 11-27). Over the next several hours, the foal could rise with assistance and would attempt to nurse, but would stop nursing shortly after beginning. Dorsal recumbency became increasingly frequent.

HISTORY AND PHYSICAL EXAMINATION

Gastric ulceration has been diagnosed in foals as young as 24 hours of age and can been seen throughout the neonatal period and beyond.[1] The incidence of gastric ulceration in foals has been cited as high as 50%

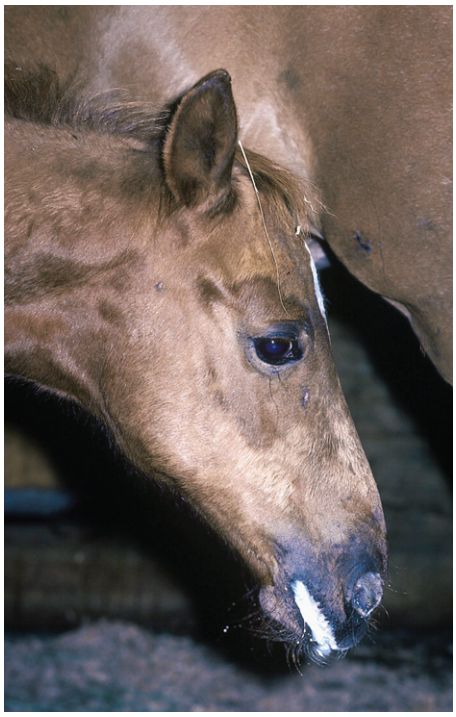

Fig. 11-27 Ptyalism in a foal with gastric ulceration.

in normal foals less than 50 days of age.[2,3] Because of this, it is difficult to know what role it plays in the health of the asymptomatic foal.[4] Stress has been implicated as a cause for gastric ulceration in the sick foal. In the neonate, ulcers are often present with concurrent diseases, such as enteritis or sepsis. The history should be utilized to determine if the foal had any prior illnesses, including diarrhea, colic, lethargy, or anorexia. Furr found that foals stressed by disease were more likely to have abnormal cortisol, T3, T4, and reverse T3 levels than age-matched normal controls foals. These stressed foals had a higher incidence of gastric ulceration than the normal foals.[4]

The clinical findings associated with ulcers can range from asymptomatic to death secondary to severe peritonitis from gastric rupture. A study in Japan of 40 foals with gastric ulceration found that the most prevalent clinical signs were depression and intermittent nursing (82.5% of affected foals) followed by diarrhea (65%), colic (37.5%), bruxism (10%), and ptyalism (7.5%).[5] Affected foals will often lay in dorsal recumbency trying to be more comfortable. Spontaneous gastric reflux from the nostrils can be seen on rare occasion. Foals with suspected or confirmed ulcers should be evaluated closely for sepsis or signs of peripartum asphyxia, as ulcers may develop secondary to these conditions. Some clinicians associate the stress of

orthopedic disease in foals to be a risk factor for the development of gastric ulcerations.

Blood and urine from '04 Belly Dancer were submitted for analysis. A complete blood count showed a mild neutrophilia of 8,343/µl and a mild hyperfibrinogenemia of 500 mg/dl. A serum biochemistry profile and urinalysis were unremarkable. Because the foal's clinical signs were compatible with gastric ulceration, gastroscopy was performed. Hemorrhagic ulcers in both the squamous and glandular portions of the stomach were found. The duodenum and esophagus appeared unaffected. Abdominal ultrasonography was performed and the results were unremarkable. Abdominal radiography revealed mild to moderate gas distention of the intestines.

DIAGNOSTICS

Because of the role that other diseases may play in the development of gastric ulcers, the diagnostics surrounding the neonate with gastric and/or duodenal ulceration should include a thorough investigation of the systemic status of the foal, including complete blood count, serum biochemistries, and urinalysis. Blood cultures should be taken to evaluate for concurrent sepsis. Because of the potential role for hypoperfusion in the development of ulcer disease, perfusion should be monitored through serial blood pressure measurements (direct or indirect) and blood or plasma lactate concentrations.

Specific diagnostics for ulcer disease include gastroscopy or gastroduodenoscopy (including esophagoscopy for reflux esophagitis) as the most sensitive and specific means of diagnosing ulcer disease in the newborn. Usually this can be accomplished with a 1-meter endoscopy. The foal should be fasted for approximately two hours before scoping so that the gastric mucosa can be viewed better. The examination should be systematic being sure to view the distal esophagus and the squamous and glandular portions of the stomach. Lesions may vary from a mild hyperemia or gastritis to deep bleeding ulcerations (Figure 11-28, *A* and *B*). Another finding of gastroscopy in young foals is a desquamation of the squamous epithelia. This occurs in 80% of foals less than 35 days of age. Sheets of squamous epithelia shed during this time period. This can occur with or without ulceration (Figure 11-29).[6]

Radiographs of the abdomen may be useful in ruling out other causes of colic in the foal. The presence of free gas in the abdomen may be suggestive of a gastric perforation. Contrast radiography should be performed in foals with suspected gastric outflow obstruction (emptying disorders) such as those with

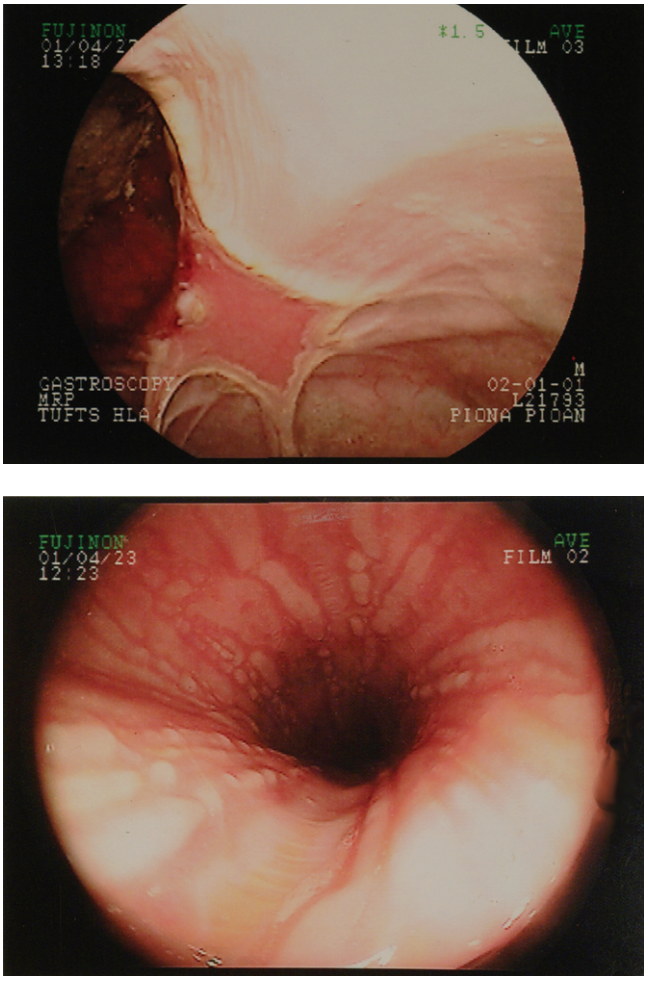

Fig. 11-28 A, Endoscopic view of ulceration of the squamous mucosa of a foal's stomach. **B,** Ulcerative esophagitis from gastric reflux. Note the "cobblestone" appearance of the mucosa.

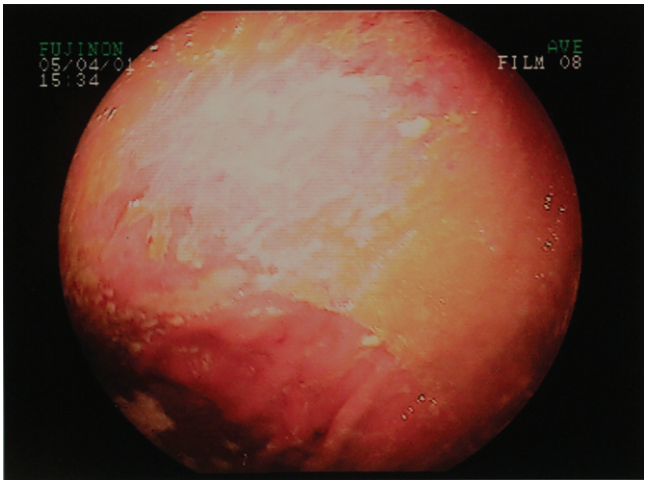

Fig. 11-29 Typical desquamation of squamous epithelia in a normal foal.

pyloric or duodenal ulceration (see Case 11-1). Delayed gastric emptying should be suspected if the barium is still in the stomach after two hours. Foals with ulcer disease should also have abdominal ultrasonography performed to evaluate for bowel wall thickness, ileus, and the possibility of peritoneal effusion. Ascites due to peritonitis in response to ulcers is a negative prognostic sign, and can mean perforation is imminent or has occurred.

Fecal or gastric occult blood may be suggestive of bleeding ulcers, but these tests are neither sensitive nor specific.

PATHOPHYSIOLOGY OF ULCER DISEASE

Neonatal ulcer disease occurs in a number of different syndromes, including silent ulcers, clinical or active ulcers, perforating ulcers, and duodenal ulcers. Silent ulcers are subclinical, but on occasion they have gone on to perforate. They may also be found incidentally on gastroscopy or postmortem examination. Clinical ulcers are consistent with the foal of this case; clinical signs included depression, partial anorexia, bruxism, ptyalism, dorsal recumbency, and colic. Ulcers can develop both in the glandular and nonglandular regions of the stomach. Duodenal ulcers, most common in the older (two- to five-month-old) foal, can result in pyloric strictures and gastric outflow obstruction and appear to represent a different syndrome than neonatal ulcers. These foals may develop reflux esophagitis as a result of the obstructive nature of this problem.

Healthy neonatal foals have an acidic baseline gastric pH, with an average pH of approximately 3.2 to 3.7.[7] They intermittently develop a gastric pH level below 1. Prolonged recumbency, greater than 20 minutes, results in a more acid gastric pH, often below 2.5 for prolonged periods.[7] Suckling milk raises the gastric pH to above 4.0, and sustains this high pH for several minutes.[7] This emphasizes the importance of frequent feedings in minimizing the potential for development of ulcers in the critically ill foal that is unable or not allowed to nurse.

The acid secretory profile of the critically ill foal is highly variable and differs widely from foal to foal. In one study, 43% of 23 hospitalized foals demonstrated alkaline profiles continuously, while another 43% had profiles typical of healthy foals.[8] The etiology of alkaline pH is unknown, but may represent parietal cell dysfunction as a consequence of hypoperfusion, or may alternatively reflect ileus with enterogastric reflux from the duodenum. Approximately 13% of foals have atypical profiles with periods of marked acidity.

The pathophysiology of gastric ulcer disease is multifactorial. In human infants, concurrent illness is strongly associated with gastric ulcers, with risk factors in some studies including mechanical ventilation (one of the most consistent risk factors), abnormal mode of delivery, delayed delivery, and hypotension.[9] Luminal factors that may predispose to ulcer formation include hydrochloric acid (HCl), pepsin, bile acids, and volatile fatty acids.[10] Additional pathophysiologic mechanisms for ulcer development include impairment of mucosal perfusion, reduction in mucus or bicarbonate secretion, neutrophil- and inflammation-mediated injury, and inhibition of nitric oxide.

Normal defenses of the mucosa vary anatomically. The squamous regions, including the esophagus, cardia, and fundus, are protected from acids by intercellular tight junctions. The glandular epithelium is protected by a mucous and bicarbonate barrier, prostaglandins, a rich mucosal blood supply, and rapid cellular restitution upon injury. Mucosal blood flow is highly dependent upon prostaglandins E1 and E2 as well as nitric oxide. Normal gastric and duodenal motility and duodenal sphincter tone are other protective mechanisms that minimize duodenal reflux of bile acids and other cytotoxins.

Ulceration in the squamous mucosa, particularly the region adjacent to the margo plicatus, must be interpreted with caution in terms of clinical significance because of the finding that up to 50% of clinically normal foals may have ulcers in this area.[2,3] Only 3% of these healthy foals had ulcers in the glandular mucosa. However, up to 40% of critically ill foals had glandular ulcers.[4] It appears that concurrent illness (sepsis, diarrhea, pneumonia) increases the incidence of glandular ulcers in the neonatal foal.

While luminal factors such as HCl may be the primary mechanisms of nonglandular mucosal injury, damage to the glandular mucosa may be multifactorial. Hypoperfusion and reduced oxygen delivery, as may occur with septic shock or hypovolemia, are believed to be important in the pathogenesis. Hyposecretion of sodium bicarbonate or mucus is also important, and these often occur secondary to hypoperfusion. Inflammatory mediators also play a role in mucosal injury. The use of nonsteroidal anti-inflammatory drugs, such as phenylbutazone, may lead to gastric ulceration as a consequence of prostaglandin E inhibition, leading to a reduction in mucosal blood flow, and bicarbonate or mucus secretion.[11,12] Candidiasis has been associated with gastric ulcers in neonatal foals, however in the author's opinion it is not clear whether they were primary or secondary invaders.[13]

'04 Belly Dancer was treated with a combination of supportive intensive care and gastric protectants. Supportive care consisted of crystalloid administration and parenteral dextrose administration, with a conservative approach to enteral feeding. Blood pressure was monitored

Table 11-3 Antiulcer Medication for Foals

Drug	Dosage	Action
Sucralfate	10–20 mg/kg PO q 6–8 h	Mucosal adherent
Cimetidine	20 mg/kg PO q 6–8 h 6.6 mg/kg IV q 6 h	Histamine-2 antagonist
Ranitidine	6.6 mg/kg PO q 8 h 1.5 mg/kg IV q 8 h	Histamine-2 antagonist
Famotidine	2.8 mg/kg PO q 12 h 0.3 mg/kg IV q 12 h	Histamine-2 antagonist
Omeprazole	4 mg/kg PO q 24 h	Proton pump inhibitor
Metaclopramide	0.02–0.04 mg/kg/hour CRI	Prokinetic drug

and maintained with crystalloid therapy. Urine output was also monitored closely as a marker of renal perfusion. The foal was fed a combination of goat milk and mare's milk replacer through a small indwelling nasogastric tube. A total of 10% of body weight was fed per day, divided into small feedings every two hours. The foal was evaluated for gastric residuals via aspiration on the nasogastric tube with a syringe. Ceftiofur (6 mg/kg, IV) was administered because of the possibility of concurrent sepsis.

For ulcer treatment directly, omeprazole (4 mg/kg PO, q 24 h) was initiated. Oral sucralfate was also administered (20 mg/kg, PO, q 6 h). The sucralfate and omeprazole were staggered by several hours to prevent nonspecific binding of the omeprazole by sucralfate.

TREATMENT

Treatment of the neonatal foal with gastric ulcer syndrome consists of supportive care and the use of antiulcer medications. Supportive care consists of maintenance of fluid volume, pressure support, and supplementation of oxygenation through insufflation as necessary for hypoxemia. Acid-base and electrolyte disorders should be corrected. Antimicrobials should be administered to treat and/or prevent sepsis in the neonate. Nutritional support is also critical to the management of the neonate with gastric ulcers. Small, frequent meals of milk should be provided in order to buffer gastric acids and to maintain higher intraluminal pH.[7] Continuous rate infusions of milk can also be provided, but caution must be taken that the foal's stomach does not become overdistended.[14] The nasogastric tube should be intermittently checked for gastric residual accumulation.

Specific therapy of gastric ulcers includes mucosal adherents, histamine type 2 receptor antagonists, and proton pump inhibitors. Sucralfate, a hydroxy aluminum salt of sucrose called sucrose octasulphate, is a mucosal adherent. At acid pH (<2), sucralfate forms a viscous gel that binds ulcers. Sucralfate also inhibits pepsin, buffers acid, and stimulates the production of prostaglandin E. This latter action stimulates bicarbonate and mucus secretion.[10] Sucralfate also binds epidermal growth factor and thus may play a role in epithelial restitution. Suggested doses for sucralfate include 10 to 20 mg/kg PO q 6 to 8 h (Table 11-3).

Histamine-2 antagonists include cimetidine, ranitidine, and famotidine. These drugs decrease acid secretion by competitively binding to the histamine receptor, thereby reducing stimulation of gastric acid secretion by histamine (see Table 11-3). Suggested dosages include the following: cimetidine 20 mg/kg PO q 6 h or 6.6 mg/kg IV q 6 h; ranitidine 6.6 mg/kg PO q 8 h or 1.5 mg/kg IV q 8 h; famotidine 2.8 mg/kg PO q 12 h or 0.3 mg/kg IV q 12 h.[15] Because cimetidine is less potent, has variable absorption in horses, and is associated with inhibition of hepatic microsomal enzymes, it may be the least preferred drug compared to the other H-2 antagonists. Intravenous or oral administration of ranitidine significantly increased intragastric pH for four and eight hours, respectively, in healthy experimental neonatal foals.[7] However, in critically ill foals, ranitidine may have a blunted duration in terms of alkalinizing response.[8] In addition, these drugs will only be beneficial when gastric pH is acidic, which may not be the case in all foals.[8] Ranitidine and sucralfate have been shown to provide partial protection against clinical, clinicopathologic, and pathologic manifestations of phenylbutazone in foals.[16]

Proton pump inhibitors have been more recently added to the treatment options for gastric ulcers in horses. The most commonly used agent is omeprazole, which decreases acid production through irreversible binding to the hydrogen-potassium ATP pump of the parietal cell. Omeprazole has been studied in healthy neonatal foals.[17,18] An oral dose of 4 mg/kg resulted in an increase in gastric pH within two hours of administration (see Table 11-3).

For foals with delayed gastric emptying, prokinetic therapy may be in order. Metaclopramide is a dopaminergic receptor antagonist that can be given as

a constant rate infusion (0.02–0.04 mg/kg/hour). Its actions are to tighten the esophageal sphincter, increase gastric motility, and relax the pyloric sphincter. Caution should be used, as overdosage can result in neurologic excitement (see Table 11-3).

While the therapy of ulcers certainly includes pharmaceuticals to raise gastric pH, prevention of ulcers through their use is controversial.[10,19] Some clinicians feel that alkalinizing the foal's stomach without evidence of ulceration may lead to increased survival of ingested bacteria and a risk of translocation of bacteria through the gastrointestinal mucosa. Also as stated above, the acid-secreting profile in the stomach of the critically ill foal may already be alkaline. Excellent supportive care along with intensive management of hemodynamics for the at-risk foal is at least as important to prevention of ulcers. Until research studies are available for defining the risks and benefits of the prophylactic use of antiulcer medications, definitive recommendations cannot be given.

'04 Belly Dancer was maintained in the hospital for approximately seven days, during which time the bruxism, abdominal discomfort, and anorexia resolved. A recheck gastroscopy prior to discharge revealed the ulcers to be healing and no longer hemorrhaging. She was discharged with instructions to continue the omeprazole for 30 days. The sucralfate was discontinued.

OUTCOME

The outcome of foals with gastric ulcers is highly variable. In a retrospective study by Taharaguchi, mortality from gastric ulceration ranged from 7.1% to 16.2% of deaths in foals between 1997 and 1999.[5] Foals with silent ulcers due to hemodynamic perturbations that go on to perforate have a grave prognosis. Foals with ulcers that do not progress to the point of perforation have a better prognosis, particularly those whose primary problem responds to therapy. Foals with duodenal ulcers have a guarded prognosis in general, because of the potential for duodenal strictures, fibrosis, and gastric outflow obstruction.[20]

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Case 11-3 | Diarrhea | Gary Magdesian

Fig. 11-30 '03 Liquid Assets, an eight-day-old Warmblood foal that presented with diarrhea.

'03 Liquid Assets, an eight-day-old Warmblood foal, was presented for lethargy, pyrexia, and signs of mild abdominal discomfort. The foal and its dam were pastured with other horses and one additional foal that were reportedly healthy. The foal had been clinically normal since birth. Gestation and parturition were unremarkable. The foal had been nursing well until that afternoon, when he preferentially sought out water. The owner monitored the foal's temperature that afternoon, and noted fevers as high as 103° F.

On presentation to the Veterinary Medial Teaching Hospital, the foal was found to be lethargic, alert, and ambulatory. A systemic inflammatory response syndrome was evident, as it was tachycardic (p = 115 beats/minute), tachypneic (80 beats/minute), and febrile (T = 102.2° F). The foal's body condition score was estimated to be 4/9, and mild abdominal distention was present. It was estimated that the foal was 5% dehydrated. Yellow mucoid feces were passed during the examination (Figure 11-30).

HISTORY AND PHYSICAL EXAMINATION

The peripartum history and history of the days prior to the development of diarrhea are important in differentiating the causes of diarrhea in foals. The potential for peripartum asphyxia, immature gestational age, and sepsis can be assessed through history. Foals with perinatal hypoxic-ischemic injury are at significant risk for gastrointestinal dysfunction, including diarrhea. Premature foals are predisposed to necrotizing enterocolitis. Additional information that is pertinent to the workup and support of the diarrheic foal include nursing ability and appetite, mentation and activity level, housing environment, and character and frequency of the diarrhea. Assessment of passive transfer of colostral antibodies is also important, as foals with failure of passive immunity are at increased risk of developing sepsis and possibly infection with pathogenic enteric organisms. On the other hand, foals with high intakes of colostrum and milk may be at increased risk for clostridial enteritis, as it has been hypothesized that colostral trypsin inhibitors may protect clostridial toxins from acid degradation in the stomach. Ingestion of large quantities of milk from heavy lactating mares may provide for additional enteral substrate for proliferation of clostridial organisms. Additional historic information centers on diet. Foals provided milk replacer or a nonequine source milk rather than mare's milk are at increased risk for development of osmotic diarrhea. Foals from poor milkers may be ingesting water or foreign material such as dirt or bedding and are at risk for diarrhea associated with pica.

Some level of epidemiologic data is also very useful in determining the etiology of diarrhea in foals. Information as to whether the foal is part of an outbreak situation (suggesting an infectious, nutritional, or toxic cause) or the sole foal with diarrhea on a farm is useful in directing the diagnostic approach. Hygiene and husbandry practices should be assessed for aiding in education toward minimizing the incidence of diarrhea on farms. Stall versus pasture housing and number of foals per paddock or pasture should also be considered.

Neonatal foals can present with diarrhea at any age between hours and several days of age. Early diarrhea is consistent with hypoxic-ischemic damage or sepsis. Diarrhea in the slightly older foal is indicative of infectious or dietary causes. The neonate with diarrhea should be evaluated for the following: 1) circulatory volume and hydration status, 2) clinical signs consistent with systemic inflammation (e.g. SIRS, sepsis) such as mucosal hemorrhages, congested or hyperemic mucous membranes, injection of vessels, tachycardia, tachypnea, or fever, 3) nutritional status through assessment of body condition or weight, and 4) indicators of concurrent disease such as bacteremia, signs of asphyxial injury, or congenital defects.

Circulatory status should be assessed in the physical examination by close attention to mentation status, capillary refill time, jugular vein fill time, extremity temperature, mucous membrane color, heart rate, and pulse quality. Heart rate can be misleading in the

Table 11.4 Causes of Neonatal Diarrhea

Bacterial	Viral	Parasitic/Protozoal	Environmental	Other
Clostridium perfringens	Rotavirus	*Cryptosporidium*	Pica	Foal heat diarrhea
Clostridium difficile	Coronavirus	*Strongyloides westeri*	Overfeeding	Prematurity (necrotizing enterocolitis)
Salmonella		*Giardia*	Improper mixing of milk replacer	Gastric ulcers
Sepsis		*Eimeria*		Hypoxic-ischemic injury
				Lactose intolerance

neonatal foal, however, as those with hypoxemia, hypothermia, or hypoglycemia can be bradycardic despite significant hypovolemia. Hydration status, reflecting interstitial and intracellular volumes, is indicated by skin turgor, mucous membrane texture, sunken eyes, and corneal quality. The abdomen should be evaluated for distention. Ballottement can indicate ascites or gas distention. The perineum should be assessed for scalding and dermatitis associated with fecal adherence to hair and skin. A cautious digital examination can reveal sand or dirt, rectal impactions, and rectal edema. Body condition scoring can be performed in the neonatal foal, and a subjective evaluation should be performed as a minimum because many diarrheic foals lose substantial amounts of weight (see Chapter 4).[1] Because foals with enterocolitis are at risk for bacterial translocation and subsequent sepsis, they should be evaluated for signs of localized sepsis such as effusive joints or enlarged external umbilical stumps.

PATHOGENESIS

The pathophysiology of diarrhea is multifactorial. Factors resulting in diarrhea from enterocolitis include hypersecretion, osmotic draw, altered motility, altered Starling's forces (as with increased vascular permeability or hydrostatic pressure, or decreased colloid osmotic pressure), maldigestion/malabsorption, and inflammation. Though one mechanism may predominate in some forms of diarrhea, most of them contribute.

Foals with enterocolitis often exhibit signs consistent with abdominal pain. Differential diagnoses that should be considered in foals with acute abdominal disease include strangulating and nonstrangulating obstructions, uroabdomen, and other nongastrointestinal causes of colic, such as liver disease. Foals with impending enterocolitis can be very difficult to differentiate from those with obstructive diseases, because they often exhibit signs of abdominal pain and distention prior to the onset of diarrhea. The presence of fever and leukopenia are suggestive of enterocolitis, but not specific. Abdominal ultrasonography and radiography can help in differentiation of these conditions.

Causes of diarrhea in neonatal foals include both infectious and noninfectious causes. Noninfectious causes include "foal heat diarrhea," pica, dietary intolerance, gastric ulcer disease, hypoxic-ischemic injury, and necrotizing enterocolitis. Infectious causes include bacterial, viral, parasitic, and protozoal causes (Table 11-4).

Foals with foal heat diarrhea are otherwise bright and nursing well. They do not experience a systemic inflammatory response, and therefore have normal hematologic and vital sign findings.[2,3] The name *foal heat diarrhea* is a misnomer because the diarrhea does not appear to be a result of hormonal changes in the mare.[3] Rather, it is a result of intestinal maturational changes. It usually occurs between seven and 10 days of life and is self-limiting.

Pica results from ingestion of sand, dirt, bedding, or hair.[4] Inflammatory or motility alterations secondary to the presence of foreign material can result in obstructions or impactions as well as diarrhea. Another dietary cause of diarrhea in the foal is dietary intolerance. It occurs when either a foal is lactose-intolerant (secondary to infectious diarrheas such as clostridiosis or rotaviral infection) or is an orphan foal with diarrhea resulting from feeding excessive amounts of milk replacer or milk replacers mixed at higher than 11% total solids.[5] Milk replacers with sucrose or maltose are particularly offensive.[5]

Gastric ulcer disease is associated with diarrhea in some neonatal foals. Clinical signs can be inapparent or include bruxism, ptyalism, dorsal recumbency, diarrhea, or colic (see Case 11-2). Hypoxic-ischemic insult as occurs with peripartum asphyxia can result in gastrointestinal injury, leading to diarrhea. Hypoxic and subsequent reperfusion injury may both contribute to mucosal compromise. Smooth muscle and serosal dysfunction may also result. Energy depletion as occurs secondary to hypoxic-ischemic injury leads to cell membrane pump failure. Subsequent reperfusion injury leads to oxidant injury as well as inflammatory cell activation and "no-reflow" phenomenon.

Necrotizing enterocolitis (NEC) is a state of gastrointestinal necrosis that occurs from mucosal injury, as might occur with asphyxial injury, the presence of enteral nutrition, and bacterial invasion of the GI wall. Ileus, gastric reflux, abdominal distention, intestinal perforations, or diarrhea can result from NEC.[6] Prematurity is a risk factor for development of necrotizing enterocolitis.

Infectious causes of diarrhea often occur in large groups of foals that are housed together; sporadic cases can also occur, particularly with clostridial agents. Viral etiologies include rotavirus and coronavirus. Rotavirus infects and denudes small intestinal microvilli, resulting in maldigestion and malabsorption.[7] It thus interferes with lactase function and sodium-glucose cotransport. Because of relative sparing of crypt epithelium, the virus also results in increased net secretion. Clinical signs vary from mild to severe diarrhea, requiring minimal to intensive therapeutic intervention, respectively. Experimentally, the incubation period is as short as two days.[7] Most affected foals are five to 35 days of age, although younger and older foals can be affected. Older foals (up to 60 days of age) usually have mild diarrhea, and asymptomatic animals can shed the virus.[7,8] Vaccination of gravid mares may reduce the incidence of disease on farms, as well as the severity of clinical signs.[9,10] Phenolic compounds are the optimal disinfectant type used, as rotavirus is resistant to many others. Coronavirus has been associated with diarrhea in foals.[11,12] It infects the small intestine during the first few days of life, with persistence of viral antigen in the crypt cells for three to four days after onset of diarrhea.[11] Complications of coronaviral infections can include coronitis and limb edema associated with inadequate perfusion of the extremities.[11] Other potential viral etiologies of diarrhea include adenovirus and parvovirus, although their exact role in foal diarrhea has not been clearly defined.[13]

The most common bacterial causes of diarrhea include clostridial agents, especially *Clostridium difficile* and *C. perfringens,* and *Salmonella.* The clostridial infections can result in outbreaks or sporadic cases of diarrhea. *C. difficile* is a primary pathogen in neonatal foals and does not require prior antimicrobial administration as a risk factor for development of diarrhea as is usually the case with adult horses.[14,15] The primary virulence factors for pathogenicity include two large exotoxins, toxins A (enterotoxin) and B (cytotoxin). *C. difficile*–associated disease ranges from mild diarrhea to highly fatal, hemorrhagic, or necrotizing diarrhea.[16] It has also been associated with lactose intolerance in foals.[14] It should be noted that toxigenic *Clostridium difficile* can be cultured from the feces of clinically normal foals, just as it can from healthy infants, and it is unknown what circumstances or agent-host interactions lead to clinical disease.[17,18]

Clostridium perfringens types A and C have been reported to cause enterocolitis and diarrhea in neonatal foals. As with *C. difficile,* the pathogenicity of *C. perfringens* A and C is dependent upon virulence factors, especially the production of enterotoxins.[19] In a recent epidemiological study, *C. perfringens* was found in 90% of normal three-day-old foals and 64% of normal foals at eight to 12 hours of age. The most common genotype was type A (85%), and *C. perfringens* type C was found in less than 1% of the foals. These results suggest that type A is likely part of the normal microflora of the neonatal foal (and thus the clinical relevance of positive cultures without presence of enterotoxin are questionable), whereas Type C is rarely found in the normal neonatal and has been associated with the clinical signs of watery to hemorrhagic diarrhea, but also includes abdominal distention, colic, and ileus.[20] Therefore, typing of isolates is critical to pursuing positive cultures, because the type of *C. perfringens* varies between clinically normal and affected foals. Foals with *C. perfringens,* type C *infection* can develop rapidly progressive obtundation and colic and may die before the onset of diarrhea. *C. perfringens*–associated diarrhea is associated with a high mortality rate, 54% in one study, and is highly associated with fatal diarrhea in another study.[8,19] Adult horses may serve as reservoirs for spores in the environment.

Salmonellosis is another bacterial form of enterocolitis that can affect the neonatal foal as it can adult horses. Concurrent sepsis is a concern with salmonellae, due to invasiveness and the potential for translocation across the compromised gut barrier. Studies have found an association between isolation of salmonellae from foals with diarrhea and fatality.[8] The severity of the disease, in part, relates to the serotype involved, with group B salmonellae, such as *S. typhimurium,* being among the most pathogenic. Salmonella of other groups can also cause disease, for example, a group C1 *Salmonella ohio* has been reported to cause an outbreak of neonatal salmonellosis.[21] Mares of infected foals may be asymptomatic carriers of Salmonella and the source of the foal's infection. Other bacteria that can cause diarrhea sporadically in the neonate include *Actinobacillus sp.* (in association with bacteremia), enterotoxigenic *E. coli, Bacteroides fragilis, Clostridium sordelli, Aeromonas hydrophila,* and *Streptococcus durans.*[22-27] The significance and pathogenesis of these agents in neonatal foal diarrhea requires further study.

The primary parasitic agent that has been associated with diarrhea in the young foal is *Strongyloides westeri.*[8] It appears that heavy infestations with more than 2000 eggs per gram of feces are required for development of diarrhea, and it is generally not a cause of severe

diarrhea.[8] *Strongyloides westeri* is transmitted to foals through suckling milk.

The primary protozoal enteric pathogen of foals is *Cryptosporidium parvum.* It was initially believed that *Cryptosporidium* infections were limited to immunocompromised foals such as Arabians with severe combined immunodeficiency syndrome.[28] More recently, it has been identified as a pathogen of immunocompetent foals as well.[29] The organism invades the microvillus, occupying an intracellular but extracytosolic space. It thus causes villus blunting and maldigestion with a secondary osmotic diarrhea. Most affected foals are five days of age and older, but younger foals can develop disease with high-level exposure. Diarrhea usually lasts between five and 14 days, with recovering animals and asymptomatic older foals and adult horses shedding oocysts. One study identified *Cryptosporidium parvum* causing an outbreak of neonatal diarrhea to be genotypically identical to that associated with bovine diarrhea.[30] However, exposure to cattle was not found to be an important source of infection for foals in another epidemiologic study.[29] Sources of cryptosporidial infection in foals have not been definitively elucidated.[29] Mares, cattle, and municipal water sources have all been suspected as the source of infection in foals, but these remain speculative.[29] Because of the zoonotic risk associated with *Cryptosporidium,* affected foals should be handled carefully with particular attention to good hygiene. The role of other protozoal agents, including *Eimeria leukarti, Trichomonas equi,* and *Giardia sp.,* is poorly understood and requires further study.

A complete blood count from '03 Liquid Assets revealed hyperfibrinogenemia (500 mg/dl) with a normal leukocyte count. A serum biochemical profile was unremarkable except for mild hyperchloremia (105 mEq/liter). Venous blood lactate concentration was mildly increased at 2.1 mmol/liter. Venous blood gas analysis was otherwise unremarkable. Whole-blood immunoglobulin concentration was found to be 400 to 800 mg/dl using a commercial immunoassay (SNAP test: IDEXX Laboratories, Inc., Westbrook, ME). Abdominal ultrasonography revealed multiple distended, fluid-filled small-intestinal loops that were initially hypermotile, and later hypomotile. Thoracic radiography was unremarkable.

Daily fecal cultures for* Salmonella sp. *were negative. Immunoassays for* Clostridium difficile *toxin A were negative, as was fecal culture for* C. difficile. *Electron microscopy of feces was negative for viral particles, as was a fecal ELISA for rotavirus. Fecal flotation was negative for nematodes. An immunofluorescent antibody (IFA) assay was positive for large numbers of* Cryptosporidium *oocysts. An IFA for* Giardia sp. *was negative.

DIAGNOSTIC TESTS

The clinical pathology of foals with diarrhea can vary depending upon whether there is a concurrent systemic inflammatory response syndrome. The hematologic (CBC) findings can vary from unremarkable to those of hemoconcentration, leukopenia, and hypoproteinemia. A left shift with immature (band, metamyelocytes) neutrophils, with variable toxic cytologic changes, may also be present, reflecting a profound inflammatory response such as sepsis. Hypoproteinemia often reflects protein-losing enteropathy, and hyperfibrinogenemia may be present in the face of inflammatory mediators induced by endotoxemia. Thrombocytopenia occurs when coagulopathies such as disseminated intravascular coagulation are triggered.

As for hematology, serum biochemistry analyses are normal when diarrhea occurs without gastrointestinal inflammation. Enteritis or enterocolitis with subsequent activation of SIRS can lead to organ dysfunction as might occur with severe sepsis. Increases in creatinine and/or BUN and liver enzymes or bilirubin concentrations reflect renal or hepatic dysfunction, respectively. Hypoalbuminemia usually reflects gastrointestinal protein loss. Similarly, hypoglobulinemia may be present, although it may be due to failure of passive transfer of colostral antibodies as well as GI loss. A variety of electrolyte derangements may reflect enteric losses, renal dysfunction, or acid-base derangements and often include hyponatremia, hypochloremia or hyperchloremia, hypokalemia or hyperkalemia, and an increased anion gap. Decreases in total CO_2 concentrations reflect metabolic acidemia. Anion gap may also be increased with hyperlactatemia.

Metabolic acidemia results from both organic and inorganic acidosis. Lactate is the primary organic anion contributing to acidemia. Hyperlactatemia results from a combination of hypoperfusion associated with hypovolemia and hypotension, hypermetabolism, increased glycolysis from inhibition of pyruvate dehydrogenase by inflammatory mediators, enhanced activity of Na-K ATPase due to circulating catecholamines, and reduced hepatic or renal clearance of lactate. Inorganic causes of acidemia in diarrhea cases include hyponatremia or hyperchloremia resulting in a decrease in strong ion difference. The acid-base status is reflected on blood gas analyses as reduced pH and increased base deficit.

As part of intensive management of foals with severe enterocolitis, additional diagnostic monitoring should include indirect blood pressure, urine output measurements, and urinalysis with fractional excretion of electrolytes. Because foals with diarrhea and

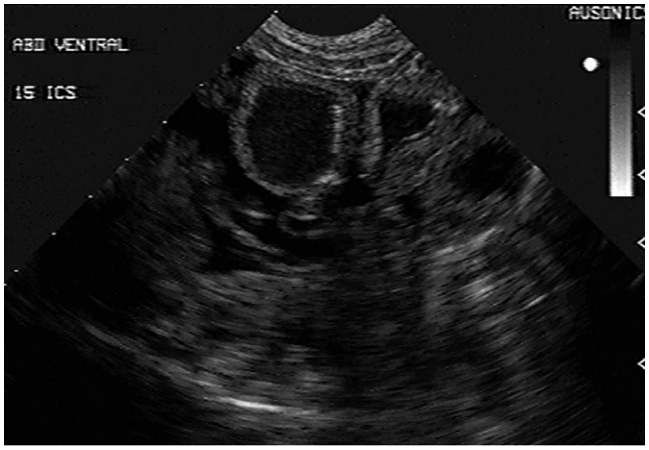

Fig. 11-31 Ultrasound image of dilated small intestine. Note the thickened wall and distended luminal diameter.

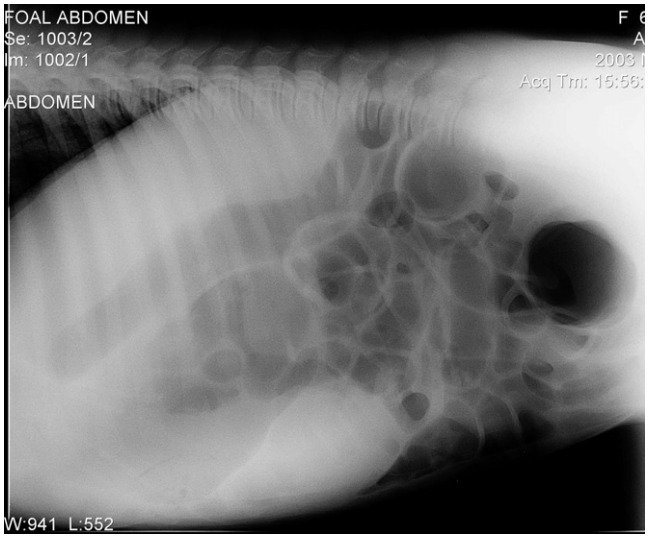

Fig. 11-32 Abdominal radiographs of a foal with diarrhea. Note the distended small and large intestine.

SIRS are at risk for coagulopathies, monitoring should also include clotting times (PT, aPTT) and measurement of fibrin degradation product or D-dimer concentrations. Antithrombin concentrations may be low because of induction of coagulopathies or loss of this small protein through the compromised GI mucosa.

Imaging should be a part of the diagnostic workup of these foals with diarrhea. Abdominal ultrasonography and radiography can aid in differentiating causes of acute abdominal disease. Ultrasound evaluation should include assessment of bowel wall thickness, luminal diameter, and small-intestinal motility (Figures 11-16 and 11-31). Ascites or effusion can also be detected. Radiography can be utilized to assess the degree of gastrointestinal distention (Figures 11-9, 11-12, and 11-32). It can also be utilized to detect pneumatosis intestinalis, or linear gas shadows within the wall of the GI tract, a hallmark of necrotizing enterocolitis. Sand and radiopaque foreign material will also be apparent on abdominal radiographs.

Table 11.5 Specific Diagnostic Tests for Diarrhea

Etiology	Diagnostic Test
Rotavirus	Electron microscopy, ELISA
Salmonella	Fecal culture (five samples) or PCR, test mare as well
Clostridium perfringens	Fecal culture with PCR typing, Gram-stain feces, toxin assay
Clostridium difficile	Fecal culture, toxin assay
Cryptosporidium	Immunofluorescence assay, acid-fast stain, flow cytometry
Strongyloides westeri	McMaster fecal flotation method
Lactose intolerance	Lactose tolerance test

Specific diagnostic evaluation of the neonatal foal with diarrhea includes a number of tests to rule out pathogenic agents (Table 11-5). Fecal samples can be screened for viral particles with electron microscopy. Fecal ELISA and immunoassays are available for rotavirus and coronavirus. Fecal cultures can be performed for *Salmonella sp.* and clostridial organisms. To increase the sensitivity of identifying salmonella shedders, repeated daily cultures should be performed (up to five consecutive samples). Alternatively, PCR techniques are available for salmonellae, although the findings must be interpreted in light of the high-level sensitivity of this test.

Positive cultures for *C. difficile* and *C. perfringens* must be interpreted with caution as nontoxigenic and incidental colonization is possible. The diagnosis of *C. difficile*–associated disease should be coupled to toxin assays. Commercial immunoassays test for toxin A or both toxin A and B. These kits are easy and rapid, however they have variable sensitivities. Stool cytotoxin assays for toxin B are also available and are considered the gold standard for toxin testing, but are time-consuming. PCR techniques for *C. difficile* toxin gene sequences are currently moving from the experimental arena to the clinical setting. Diagnosis of *C. perfringens* enterocolitis is difficult to make. Unfortunately, immunoassays are not available for most toxins, except for enterotoxin. Therefore, cultured isolates must be typed using PCR techniques, such as the multiplex PCR. The diagnosis is made from positive cultures of toxigenic and pathogenic isolates of *C. perfringens* (e.g., type A or C), as well as exclusion of other pathogenic agents. Gram staining of feces can serve as a rapid screen for clostridial overgrowth, however this technique is neither sensitive nor specific (Figure 11-33).

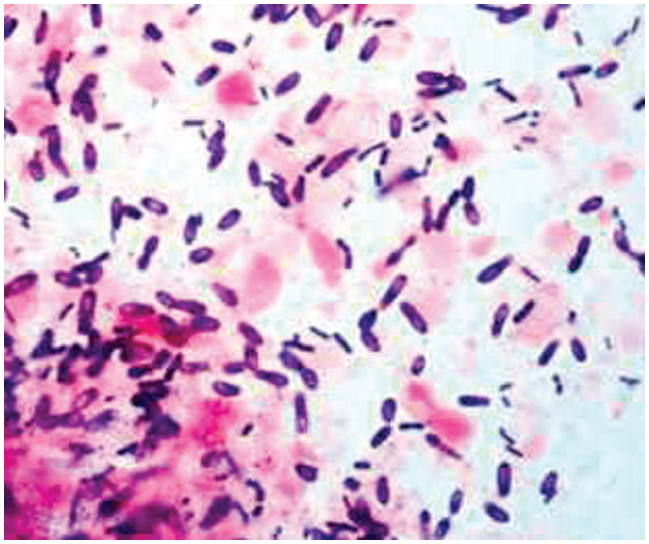

Fig. 11-33 Gram staining of diarrheic feces caused by *Clostridia sp.* may show an increased number of Gram-positive rods.

There are a number of diagnostic tools available for diagnosis of *Cryptosporidium parvum* infection. Immunofluorescence assay (IFA), acid-fast (AF) staining, and flow cytometry have been developed for identification of oocysts.[29] In one study, AF and flow cytometry were determined to be more sensitive than IFA.[29] AF staining was less specific, however. Because of their small size, oocysts are very difficult to visualize microscopically after fecal flotation. Fecal flotation is useful for identifying *Strongyloides westeri* ova, with the McMaster method used for quantification.

If one is concerned that lactose intolerance is playing a role in the continuation of a foal's diarrhea, then the use of a lactose tolerance test may be indicated. After a four-hour fast, the foal is administered lactose (1 g/kg) through a nasogastric tube. Blood samples collected in fluoride oxalate tubes are taken for glucose levels at preadministration, immediately postadministration, and every 30 minutes for three hours. A normal absorption curve would show a doubling of glucose in 60 to 90 minutes. An absence of increase in glucose or a delay in the increase would indicate a problem with lactose digestion and absorption.[31]

Therapy for '03 Liquid Assets was initiated with replacement crystalloid therapy. The foal was rehydrated with Plasma-Lyte 148, and dextrose supplementation was provided through 5% dextrose in water. After rehydration, maintenance fluid requirements were met with Plasma-Lyte 56. Over time the foal developed an inorganic acidosis (hyponatremia, hyperchloremia), which was managed with administration of isotonic sodium bicarbonate. Immunologic and colloid support was provided with a plasma transfusion (2 liters total). With time, the foal developed increasing abdominal distention associated with ileus. To minimize distention and abdominal discomfort, the foal was kept nothing per os and not allowed to nurse. Nutritional support was provided in the form of parenteral nutrition, consisting of a combination of dextrose, intralipid, and amino acid solutions.

Antimicrobial therapy was instituted as a means of preventing bacterial translocation and bacteremia. Ceftiofur (10 mg/kg, IV, q 12 h) and amikacin (21 mg/kg, IV, q 24 h) were administered to provide broad-spectrum antimicrobial coverage with potent Gram-negative efficacy. Kaolin pectate and bismuth subsalicylate were utilized intermittently as gastrointestinal protectants.

As the foal's abdominal distention and ileus improved, lactase enzyme (3000 U, PO, q 4 h) was provided as enteral feeding was reintroduced and gradually advanced, because of suspected lactose intolerance. As enteral feeding was tolerated, the foal was allowed to nurse the mare for increasing lengths of time and increasing frequency. Intravenous fluid therapy was gradually reduced. The GI motility improved over the next several days as the foal's abdominal distention resolved and fecal character improved. The foal was discharged after eight days of hospitalization.

TREATMENT

The treatment of foals with diarrhea is highly variable, depending upon the severity of clinical signs and physiologic derangements. In general, the management of enterocolitis includes a number of goals. These include hemodynamic, metabolic, and nutritional support; gastrointestinal protectants; antibiotic coverage; and infectious disease control. If a specific agent is identified, then specific therapy for that agent can be instituted.

Hemodynamic disturbances are common among foals with enterocolitis, particularly those with SIRS or sepsis syndrome. Hypoperfusion results from hypovolemia, altered myocardial contractility, inappropriate vasomotor responses, and hypooncotic states associated with hypoalbuminemia. Hemodynamic support occurs primarily in the form of intravenous fluid therapy, consisting of both crystalloids and colloids. A number of crystalloids are appropriate for foals with diarrhea, but because of the tendency for metabolic acidemia, fluids with higher strong ion differences such as Normosol R, Plasma-Lyte 148, or lactated Ringers solution are more ideal than 0.9% saline.[32]

Volume replacement in the neonatal foal should be done with great attention; overzealous administration of crystalloids may potentiate gastrointestinal edema. Monitoring of central venous pressure, urine output, and serial lactate concentration measurements can aid

in guiding volume replacement. Colloid therapy is indicated in the hypooncotic and hypovolemic foal. Plasma or synthetic colloid solutions, such as hetastarch, can be used. Plasma has the advantages of providing not only albumin, but also immunoglobulin, antithrombin, clotting factors, and other proteins. If hetastarch is used, platelet counts and clotting times should be monitored, as coagulopathies associated with reduced concentrations of von Willebrand's factor and factor VIII may develop. Once volume replacement has occurred and the central venous pressure (CVP) is at maximum (10 cm H_2O), hypotension should be addressed with inotropes, such as dobutamine (2 to 20 µg/kg/minute, IV CRI). If hypotension and clinical parameters of hypoperfusion persist after initiation of inotropy, then vasopressors should be considered (norepinephrine or vasopressin CRI—see Chapter 7).

Metabolic support occurs in the form of managing acid-base and electrolyte balance. Metabolic acidemia is treated depending upon the cause of acidosis; organic acidoses (lactic acidosis) should be treated with optimizing peripheral oxygen delivery. Inorganic acidoses, as occur with hyponatremia or hyperchloremia associated with electrolyte loss into the GI tract, can be treated by correcting the underlying electrolyte disorder. Sodium bicarbonate is indicated in these situations. Potassium, calcium, and magnesium may need to be supplemented in foals with severe diarrhea. Glucose concentrations should be monitored frequently in the neonatal foal, particularly if the foal is anorexic or receiving parenteral dextrose. Both hypoglycemia and hyperglycemia should be avoided. Recently, tight glucose regulation with insulin has received a great deal of study in human critical care and is associated with improved survival in septic patients (see Chapter 7).[33] In cases with severe diarrhea, ileus and abdominal distention, abdominal discomfort, or suspected osmotic diarrhea, partial or complete withholding of milk should be considered. Parenteral nutritional support is required in these foals (see Chapter 4).

Antimicrobial therapy should be provided in order to minimize the risk for bacterial translocation across the compromised gut barrier. Broad-spectrum coverage, as with a beta lactam and aminoglycoside combination or second- or third-generation cephalosporins, is indicated (see Chapter 5). Gastrointestinal protectants include di-tri-octahedral smectite and activated charcoal, which act as adsorbents. Smectite has been shown to bind clostridial toxins in vitro.[34] However, to the author's knowledge, this product has not been evaluated in neonatal foals and should be used with caution. Other protectants include kaolin/pectin combinations and bismuth subsalicylate.

Nonspecific therapy for diarrhea may include antiulcer medication and probiotics. Sucralfate is also protective, stimulating mucosal blood flow and mucus production because of increased local prostaglandin synthesis. Treatment of gastric ulcers with proton pump inhibitors and/or histamine type 2 receptor antagonists is indicated when ulcers are suspected from clinical signs (bruxism, ptyalism, dorsal recumbency) or documented via gastroscopy (see Case 11-2). Probiotics are often utilized to modulate colonic flora. However, evidence documenting their efficacy in horses is lacking, and their use in neonatal foals prone to bacteremia warrants further study.

If a specific offending agent is identified, then treatment may be more directed. Metronidazole, administered orally or intravenously (10 to 15 mg/kg, q 8 to 12 h), is indicated in clostridiosis cases. The early use of metronidazole in even suspect cases of *C. perfringens* is important because foals can die before the onset of diarrhea. Metronidazole is also the first-line therapeutic for treating *C. difficile* infection in foals, however, cases of metronidazole resistance have been documented.[35,36] In these cases, vancomycin can be used, although it should be restricted to foals in isolation and foals that have severe clinical scores. Unfortunately, bacitracin is uniformly ineffective against equine isolates of *C. difficile*.[36,37] Ivermectin is effective in treating *Strongyloides westeri* infestations.[38] Paromomycin has been suggested as a treatment for *Cryptosporidium* infections, although its efficacy and safety are unproven in foals.[39] Exogenous lactase enzyme (3000 to 6000 U/50 kg foal, PO, q 3 to 6 h) should be provided to foals with rotaviral, cryptosporidial, and streptococcal infections and those with osmotic diarrheas to aid in digestion and prevention of chronic osmotic diarrhea.

Nursing care is very important for the diarrheic neonate. Cleanliness and hygiene are important not only for infectious disease control, but also for preventing secondary complications such as thrombophlebitis in the patient. The foal with diarrhea should be isolated so as to prevent spread of infectious agents. Consideration must be given to efficacy of particular disinfectants for specific agents. Though bleach is effective against most pathogens, rotavirus is best killed with phenolic compounds. *Cryptosporidium* is resistant to most disinfectants. High heat and ultraviolet light may be helpful in eliminating this organism.

Owners should be warned about the potential zoonotic nature of *Salmonella* and *Cryptosporidium.* Frequent handwashing and use of separate clothing when working with sick foals are prerequisites of curtailing the spread of the infection. *Cryptosporidium* can also cause disease through any mucous membrane contact. Protective eyewear and the use of surgical masks may be an important part of disease prevention in caretakers.

OUTCOME

Two follow-up fecal IFA tests on the foal for* Cryptosporidium *were negative. A source for the* Cryptosporidium *was not found in this case. The partial failure of passive transfer may have played a role in the pathogenesis of the disease in this case. The owner reported that the foal continued to thrive and grow one month after discharge.

The prognosis for foals with diarrhea is highly variable. Those with diarrhea and no evidence of enterocolitis have a good prognosis, while those with *C. perfringens*, some forms of *C. difficile*, and *Salmonella sp.* infections have a higher mortality rate than those with rotavirus, *Strongyloides*, or *Cryptosporidium* infections.[8]

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Case 11-4 Liver Failure in the Foal

Gary Magdesian

Fig. 11-34 '04 Jaundiced View, a 12-day-old Quarter Horse foal, presented severely depressed with intermittent seizures.

'04 Jaundiced View, a 12-day-old Quarter Horse foal, was presented for depression, intermittent seizures, icterus, and pyrexia (Figure 11-34). The foal had an unremarkable gestational length and parturition history, and had been clinically healthy until the afternoon of presentation. Approximately five hours prior to presentation, she developed acute-onset lethargy and anorexia. The foal's clinical status deteriorated rapidly, leading to seizure activity and pyrexia (104.7°F). The referring DVM administered lactated Ringer's solution, gentamicin, and ampicillin, and referred the foal.

Physical examination revealed the foal to be severely depressed and responsive only to noxious stimuli. The foal exhibited a systemic inflammatory response syndrome, with tachycardia, tachypnea, and pyrexia. Clinical signs compatible with sepsis were found on ophthalmologic exam, including yellow-discolored irides, hyphema, hypopyon, and aqueous flare. The foal was markedly icteric (mucous membranes and sclera) and was in hypovolemic shock as exhibited by prolonged capillary refill time, tachycardia, poor pulse quality, and cold extremities.

HISTORY AND PHYSICAL EXAMINATION

Important historical information for the foal with icterus and altered mentation includes farm epidemiologic data such as the number and percentage of affected foals. The spectrum of clinical signs and course of the disease encountered in outbreak situations are important, as is the age range. Administered supplements or medications should be evaluated for potential hepatotoxicity. For isolated cases, the history leading up to the disease should be investigated. Age of onset is important; for example Tyzzer's disease is limited to foals a few days of age to six weeks of age.[1,2] Management practices, including housing, diet, peripartum history, and additional concurrent disease in the herd, should be considered. Treatment prior to veterinary examination or therapies provided by the referring veterinarian, in the case of specialty practices, should be evaluated.

A detailed physical examination of the foal with liver dysfunction is important not only for elucidating the etiology, but also for management and therapy. With acute hepatic disease, foals may exhibit a systemic inflammatory response syndrome with tachycardia, tachypnea, and/or pyrexia or hypothermia. Hypovolemia and dehydration are common due to lack of nursing, third space losses (diarrhea or ascites), or vascular permeability alterations. Icterus or jaundice is a key finding with liver disease, and mucous membranes, including gingiva, vulvar, and ocular mucous membranes, as well as sclera should be evaluated closely for yellow discoloration (Figure 11-35). Fecal character should be evaluated, as some forms of liver disease can cause diarrhea or changes in fecal color. For example, foals with biliary atresia may have gray feces while those with Tyzzer's disease can exhibit diarrhea.[3-5] Abdominal distention may be present, and abdominal ballottement can be used to reveal ascites or hepatomegaly. Foals with subacute or chronic liver disease may exhibit weight loss or poor growth, which may be apparent as poor body condition. Those with

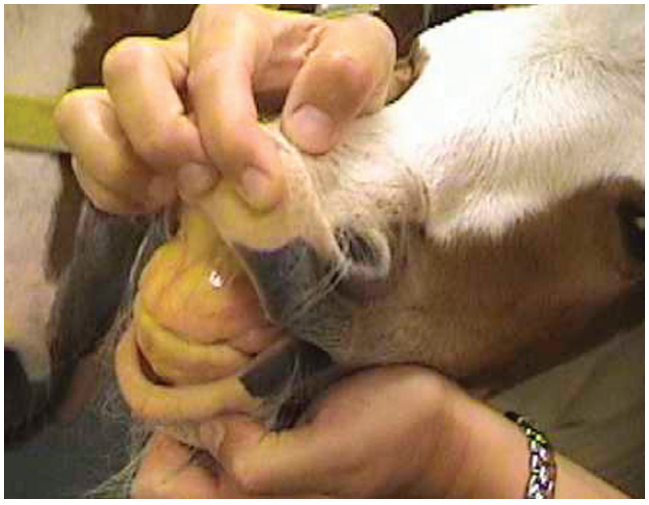

Fig. 11-35 Icteric mucous membranes are a prominent sign in both liver disease and neonatal isoerythrolysis.

acute hepatopathy, such as Tyzzer's disease, have a normal body weight and appear normal until acute onset of signs.[2,6]

The perinatal foal with hepatopathy should be closely evaluated for concurrent signs of hypoxic-ischemic injury, including encephalopathy, enteropathy, and nephropathy. Hepatic dysfunction may occur in these foals as well. Similarly, foals with sepsis can develop hepatitis.

Hepatoencephalopathy is present in many foals with acute liver disease or end-stage liver failure. Signs range from subtle to severe and fulminate. Subtle signs include mild depression and yawning. More obvious signs include central blindness, circling, head pressing, seizures, behavioral changes, and obtundation to coma.

Fundic examinations should be performed in icteric foals because herpes-positive cases often demonstrate dark and red-discolored optic discs and irregularly dilated vessels.[7]

PATHOGENESIS

The pathophysiology of liver disease in the neonatal foal is multifactorial and complex. Because of a large number of etiologies, insult or abnormalities may occur in the form of congenital, genetic, toxic, infectious, and hemodynamic causes.

The differential diagnoses for foals with icterus include fasting hyperbilirubinemia, increased erythrocyte destruction, hepatocellular disease, and cholestatic disorders. Causes of hemolysis include neonatal isoerythrolysis, drug-induced lysis, and increased red blood cell turnover from sepsis or peripartum asphyxial injury. Sepsis may impair bilirubin metabolism due to the presence of endotoxemia contributing to hyperbilirubinemia.

Liver disease occurs from a number of causes. Infectious causes include bacterial hepatitis secondary to sepsis, and infection with *Actinobacillus equuli* or *Clostridium piliformis.* Bacteremia and sepsis in general can cause hepatic dysfunction by means of inducing hypoperfusion and tissue hypoxia. Inflammatory mediators stimulated by the systemic inflammatory response syndrome (SIRS) will contribute to hepatic damage. Cholangiohepatitis from enteric microbes can result from ileus, enteritis, or ulcerative duodenitis/stricture syndrome. Bacterial hepatopathy may also occur as extension of umbilical vein phlebitis or abscessation. Hepatoencephalopathy was associated with *Rhodococcus equi* infection in one foal. Although not cultured, a liver biopsy suggested a bacterial etiology and the authors speculated that it may have been due to *R. equi* bacteremia or ascending biliary infection.[8]

Tyzzer's disease, caused by *Clostridium piliformis,* formerly known as *Bacillus piliformis,* is an acute and multifocal hepatic necrosis associated with a high mortality rate. Most commonly associated with sporadic cases on farms, outbreaks of disease can also occur. Foals present with a rapidly progressive clinical course including recumbency, hyperthermia or hypothermia, and stupor or coma, icterus, and seizures with marked hypoglycemia and metabolic acidosis.[9] Some foals may be found dead without preceding clinical signs.

Viral hepatitis from equine herpes virus 1 (EHV-1) neonatal infection can occur in association with respiratory distress, neurologic signs, and bone marrow necrosis resulting in leukopenia. Foals are infected in-utero from repeated cell-associated viremia in the dam,[9] so signs are seen immediately at birth. Icterus is a common finding in neonatal herpes infections as a result of multifocal and acute hepatic necrosis. Despite profound necrosis, liver enzymes were not increased in one retrospective report.[10] In the report, herpes-positive foals were more likely to have total white blood cell counts less than 3,000/µl and to be icteric (and hyperbilirubinemic) compared to septic or premature foals. Foals with neonatal herpes infections have a poor prognosis; however, those with milder infections may survive. Treatment with acyclovir can be attempted.[11]

Foals with hypoxic-ischemic injury from peripartum asphyxia most commonly exhibit clinical signs consistent with encephalopathy, nephropathy, or gastroenteropathy, however hepatopathies may also result. Such foals exhibit icterus from biliary stasis and hepatic dysfunction, and have increased concentrations of liver enzymes. Foals with neonatal isoerythrolysis sporadically develop hepatopathies with increases in direct bilirubin concentration in addition to indirect hyperbilirubinemia and increased liver enzymes.[12] Liver disease is suspected to occur as a result of tissue

hypoxia, iron overload from hemolysis, or bile stasis caused by the increased amounts of conjugated bilirubin.[12] Another form of liver disease occurs secondary to gastrointestinal disease, primarily strangulating or obstructive lesions and ileus. Endotoxin or bacteria can enter the portal circulation from translocation.

Congenital causes of hepatopathies include portacaval shunts and biliary atresia.[3,13] Portosystemic vascular anomalies include both intrahepatic and extrahepatic shunts.[13-15] Persistent vitelline arteries have been reported in conjunction with intrahepatic portosystemic shunts.[16] Foals with portosystemic shunts have recurrent episodes of blindness, seizures, or altered mentation associated with hepatoencephalopathy. The shunts may not be clinically apparent until affected foals are eating grain or hay. Congenital hepatic fibrosis and cystic bile duct formation is a syndrome suspected to be an autosomal recessive genetic trait of Swiss Freiberger horses.[17] This report included 30 foals that demonstrated jaundice, neurologic signs, colic, and unthriftiness.

Hyperammonemia of Morgan foals and equine glycogen storage disease IV are syndromes suspected to have a genetic basis with some degree of hepatopathy.[18-20] Persistent hyperammonemia in Morgan horses is suspected to be similar to a syndrome of hyperornithinemia, hyperammonemia, and homocitrullinuria (HHH) in humans.[18] These foals exhibit neurologic signs including seizure activity, aimless wandering, yawning, and circling. Supportive care, lactulose, and a low-protein diet resulted in temporary clinical improvement in one of two foals that was treated, however the foal relapsed and was euthanized.[18]

Glycogen-branching enzyme deficiency has been recently attributed to a mutation in the glycogen branching enzyme 1 (GBE 1) gene in Quarter Horses.[20] The syndrome has recently been termed *glycogen storage disease IV* and is believed to be inherited as an autosomal recessive trait, with clinically affected foals being homozygous for the mutation.[19,20] Affected foals are sometimes stillborn, and otherwise exhibit flexural deformities, seizure activity, respiratory or cardiac failure, or recumbency. Leukopenia, hypoglycemia, and high serum CK, AST, and GGT concentrations were common, and all foals died by seven weeks of age.[19] The livers of affected foals contained periodic acid Schiff's (PAS)-positive intracellular inclusions and no GBE activity. An additional consideration for congenital hepatic disease is hepatoblastoma.[21] Polycythemia, hyperbilirubinemia, and increased liver enzymes occur with this liver neoplasm.[21] These foals may survive to weaning or adulthood, but hepatoblastoma has been reported in an aborted fetus and may thus be congenital.[22]

Toxic hepatopathies have been reported in neonatal foals following administration of oral pastes containing ferrous sulfate in the first one to two days of life.[23] Experimental administration of iron to foals confirmed that the hepatotoxicity from the oral paste was indeed due to the contained iron.[23,24] Pathologic changes included liver atrophy, bile duct hyperplasia, lobular necrosis, cholestasis, and periportal fibrosis. Drug-induced hepatopathies can also occur during this time period because of relatively immature hepatic function and increased absorption of macromolecules during colostral IgG absorption.[12] Oral medications should be used with caution in foals less than 24 hours of age because of the potential for increased bioavailability with subsequent hepatotoxicity. Other potential hepatotoxins reported in horses include aflatoxins, pyrrolizidine alkaloids, leukoencephalomalacia, and chlorinated hydrocarbons, although these are considered unlikely in the young foal because of lack of ingestion of feedstuffs by neonates. Steroid hepatopathy has been reported in three- and 10-year-old horses, secondary to intramuscular administration of high doses of triamcinolone acetonide in both cases.[25,26]

A complete blood count from '04 Jaundiced View demonstrated hemoconcentration with a hematocrit of 46%. A mild neutrophilia was present with a toxic left shift (band neutrophils: 500/µl). Hyperfibrinogenemia was also present (600 mg/dl). A venous blood gas revealed metabolic acidemia, with a pH of 7.2 and a base deficit of 12 mEq/liter. Venous blood lactate concentration was high at 8 mmol/liter. Serum biochemistry profile showed marked hypoglycemia (28 mg/dl), and increased liver enzymes (SDH 300 IU/liter, GGT 98 IU/liter, AST 2200 IU/liter). Total, indirect, and direct bilirubin were increased as 9.1, 8.3, and 0.8 mg/dl, respectively. Blood cultures were submitted and subsequently found to be negative. Clotting profiles (PT and aPTT) were within normal limits. Blood ammonia was high at 280 mmol/liter as were bile acid concentrations (50 mg/dl).

Abdominal ultrasonography revealed generalized hepatomegaly with an increased vascular pattern, consistent with a diffuse, acute hepatopathy. Needle biopsies were taken with an automated biopsy instrument. Histopathology showed acute, multifocal, necrotizing hepatitis consistent with Tyzzer's disease. A Warthin-Starry stain (a silver impregnation technique) confirmed the presence of intracellular and filamentous rod-shaped bacteria consistent with* Clostridium piliformis *(Figure 11-36).

DIAGNOSTIC TESTS

Clinical pathologic findings in foals with liver disease include increases in concentrations of both hepatocel-

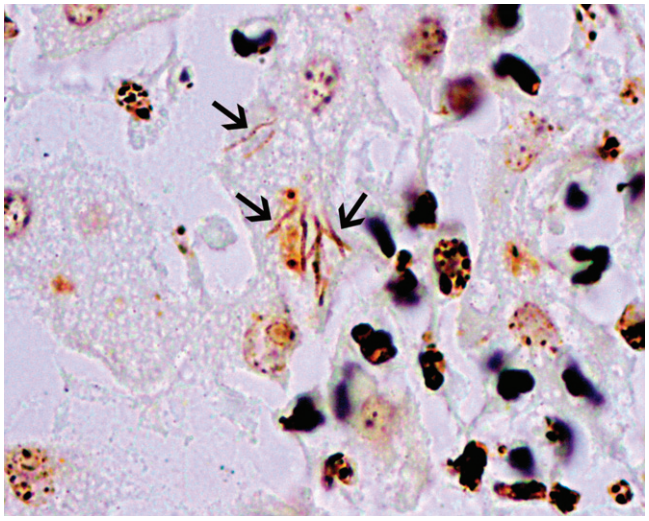

Fig. 11-36 Liver biopsy from a foal with Tyzzer's disease. Note rod-shaped bacteria. Warthin-Starry stain 100×. Courtesy of Dr. Pam Wilkins.

lular and biliary enzymes. Aspartate aminotransferase (AST) and sorbitol dehydrogenase (SDH) are examples of hepatocellular enzymes. AST is not liver-specific, however, having significant components originating from both skeletal and cardiac muscle. SDH is considered to be liver-specific and has a short (two- to three-hour) half-life. Biliary-derived enzymes include γ-glutamyl transferase (GGT) and serum alkaline phosphatase (SAP). GGT is nearly biliary-specific, however pancreatic origins must be considered when concentrations are increased. SAP has isoenzymes from multiple sources, including fast-growing bone in the neonatal foal. It should be noted that serum biochemical indicators of liver status in neonatal foals have some distinct features as compared to adult horses.[27] Serum alkaline phosphatase (152 to 2835 IU/liter), GGT (13 to 39 IU/liter), and SDH (0.2 to 4.8 IU/liter) activities are increased during the first two weeks of life.[27] Serum cholesterol, triglycerides, and total and unconjugated bilirubin concentrations peak during this same neonatal period.

Foals with cholangiohepatitis and infectious hepatopathies usually have increases of both hepatocellular and biliary enzymes. Similarly, those with toxic insults and hypoxic-ischemic disease also have increased liver enzymes. Glycogen-branching enzyme deficiency results in increased GGT concentrations. Those with portacaval shunts often have normal liver enzymes, but liver function tests are abnormal. Foals with herpes hepatopathies also usually have normal enzymes, but increased bilirubin concentrations.

Both indirect-reacting (unconjugated) and direct-reacting (conjugated) bilirubin concentrations increase with liver disease. Cholestatic disease results in increases in both components of bilirubin as well, while the percentage attributed to direct bilirubin is usually higher than with primary hepatocellular disease, often exceeding 20% to 25% of the total bilirubin concentration. On the other hand, fasting hyperbilirubinemia and that resulting from hemolysis are due exclusively to indirect bilirubin.

Serum bile acid concentrations increase with liver dysfunction, as occurs with portacaval shunts. They represent a good screening test of liver function. Bile acids, such as choleic and chenodeoxycholic acids, are synthesized by the liver from cholesterol, and are excreted into bile after conjugation with amino acids. These conjugated forms form micelles with fat in the intestine and are reabsorbed and recirculated via enterohepatic circulation. Serum concentrations of bile acids increase in the face of hepatocyte damage, biliary stasis, and shunting of portal blood to the systemic circulation as occurs with portosystemic shunts.

Hyperammonemia is often present, also reflecting liver dysfunction. The liver is the primary site of ammonia removal by converting it to urea for renal excretion. Foals with portacaval shunts commonly have high resting ammonia concentrations. Morgan foals with HHH syndrome have very high concentrations of blood ammonia (>200 µmol/liter), while liver enzymes are only mildly to moderately increased and bilirubin is normal to mildly elevated. Proper handling procedures are critical to accurate measurement and interpretation of blood ammonia.[28] Heparinized blood should be used, and the sample should be collected gently (to avoid hemolysis) and kept on ice. The sample should be run within one hour of collection or otherwise spun in order to freeze the plasma at –20° C for subsequent measurement within 48 hours. Blood from aged-matched control foals should be run concurrently.[28]

Additional biochemical indicators of liver function include serum glucose, BUN, albumin, and cholesterol concentrations. Glucose concentrations are variable, and reflect the degree of hepatic necrosis and milk intake. Foals with severe hepatitis or necrosis, such as those with Tyzzer's disease, have profound hypoglycemia. Those with portacaval shunts also commonly exhibit hypoglycemia. As BUN, albumin, and cholesterol are synthesized by the liver, dysfunction is reflected by reduced concentrations of these analytes. However, hypoalbuminemia is uncommon with liver disease, as only 18% and 6% of horses with chronic and acute liver disease had albumin concentrations below the reference value in one report.[29] It has been estimated that greater than 80% of liver mass must be lost for longer than three weeks before hypoalbuminemia develops.[30]

Fractionation of blood amino acids and determination of the branch chain amino acid (BCAA) to aromatic amino acid (AAA) ratio can aid in determining

hepatic function. Decreases in the ratio indicate insufficiency, with normal ratios falling between 3.5 and 4.5.[30] Because of liver dysfunction and reduced conversion of blood ammonia to BUN, a decrease in BUN concentration is often observed. It should be noted, however, that BUN concentrations in the normal neonatal foal are lower than those in the adult horse and low concentrations are therefore difficult to interpret in the neonatal liver patient.

Bromsulphalein (BSP) and indocyanine green are dyes that are excreted primarily by hepatic clearance. Clearance and half-life reflect hepatic excretory function and are prolonged in animals with biliary obstruction or hepatocellular failure. It should be noted that alterations in hepatic blood flow alter interpretation of BSP clearance; significant decreases in blood flow as occurs with portosystemic shunts will reduce the delivery of BSP and hence cause an increase in half-life. High bilirubin and low albumin concentrations will result in increased and decreased BSP half-life, respectively. Quantification of serum bile acids has largely replaced the use of BSP clearance as an indicator of hepatic function in horses.[30]

The concentration of triglycerides may increase in foals with liver disease because of reduced hepatic clearance and increased mobilization from adipose tissue associated with a catabolic state. Cholesterol and VLDL concentrations may decrease, however, because of reduced hepatic synthesis. It should again be noted that triglyceride and cholesterol concentrations are higher in healthy neonatal foals compared to adults, and vary with age.[27] In one report, foals had concentrations of 24 to 88 and 30 to 193 mg/dl for triglycerides in <12-hour and in one-day-old foals, respectively. Cholesterol concentrations were 111 to 432 and 110 to 562 in those same age groups.[27]

CBC findings are dependent upon the cause of liver disease. Leukocytosis may be present with cholangiohepatitis. When liver disease is secondary to sepsis or hypoxic-ischemic disease, however, leukopenia with band neutrophils is more common. Hyperfibrinogenemia is usually present with infectious or inflammatory hepatopathies, however fibrinogen may be decreased when coagulopathies such as disseminated intravascular coagulation exist.

Blood cultures should be performed in the neonatal foal with liver disease because of the possibility of sepsis causing hepatitis.

Clotting times may be prolonged with liver failure. Prolongation of prothrombin time (PT) and partial thromboplastin (PTT) occur due to a lack or reduction of synthesis of several clotting factors, including factors II, V, VII, IX, and X. This is an important clinical finding because liver biopsies may have to be delayed in hypocoagulable animals. For similar reasons, plasma antithrombin concentrations may be reduced, leading to coagulopathies such as disseminated intravascular coagulation. In one review, almost half of horses with liver disease had a prolonged PT or PTT.[31] Coagulopathies are common in horses with liver dysfunction due to concurrent systemic inflammatory response syndrome, and fibrin degradation products may be increased and thrombocytopenia may be present.

The acid-base status of foals with liver disease should be evaluated closely through blood gas analysis. With liver dysfunction, acidemia may occur as a result of increased formation and reduced clearance of organic acids such as lactate, pyruvate, and amino acids. Impaired urea synthesis may reduce renal buffering through urine acidification. Serial monitoring of lactate should be included as part of the diagnostic monitoring of the foal with liver disease because lactate clearance may be reduced.

Ultrasonography is a critical component of the diagnostic workup of foals with liver disease. It can be utilized to determine the size of the liver, changes in parenchyma, and dilated bile ducts. With infectious etiologies, such as cholangiohepatitis, hepatitis secondary to sepsis, and Tyzzer's disease, the liver appears subjectively enlarged. Biliary distention is evident in some cases. Evidence of fibrosis (hyperechogenicity) may be present in subacute to chronic cases.

Hepatic scintigraphy will confirm the diagnosis of portacaval shunts. Injection of technetium 99m-labeled sulfur colloid demonstrates alterations in blood flow or the presence of masses. Biliary scans can also be performed looking for biliary obstruction or atresia. Portograms are necessary in cases of portosystemic shunts where surgical correction is contemplated. These are done intraoperatively using radiopaque agents that are injected into a mesenteric vein with subsequent radiography. Simultaneous filling of the portal and azygous veins and caudal vena cava, and lack of intrahepatic filling indicate portacaval shunting.[30]

Histopathology provides the most specific information as to the etiology of liver disease and can aid in diagnostic, prognostic, and therapeutic directions. The safest means of performing liver biopsies is under ultrasonographic guidance and using an automated needle biopsy instrument. It should be pointed out that focal lesions such as neoplasia are easily missed by liver biopsy. Special stains (silver or Warthin-Starry stains) may be helpful in specific diagnoses such as Tyzzer disease. Fine-needle aspirates may also be helpful in the diagnosis of a specific etiology (Figure 11-37).

Culture of liver biopsies is indicated when infectious etiologies are suspected. Cholangiohepatitis is usually associated with Gram-negative enteric aerobes and Gram-negative or Gram-positive anaerobes.

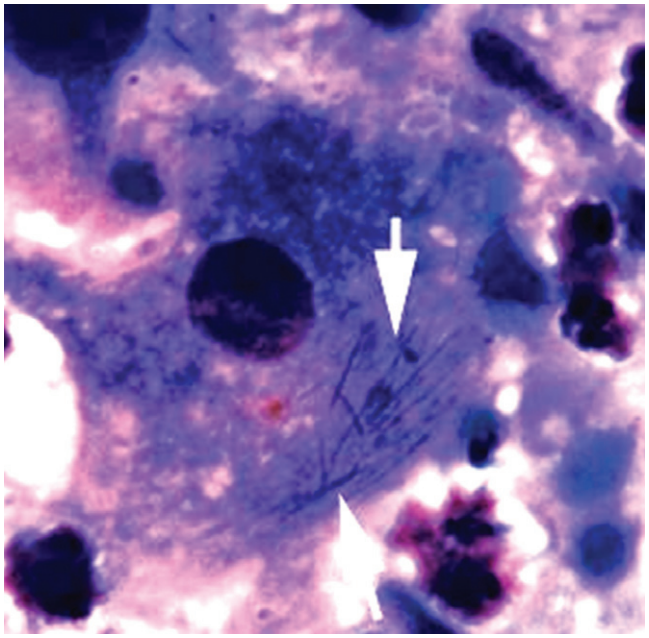

Fig. 11-37 Fine-needle aspirate from the liver of a foal with Tyzzer's disease. Note intracellular rod-shaped bacteria. Courtesy of Dr. Michelle Barton.

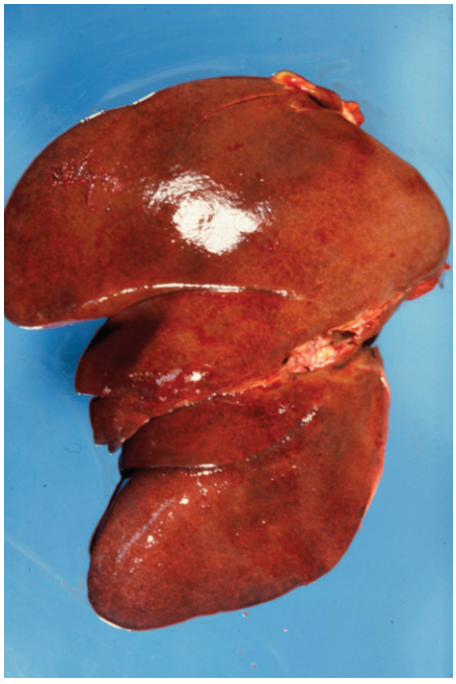

Fig. 11-38 Hepatomegaly is a prominent sign of Tyzzer's disease.

Pathogenesis of and Clinical Findings in Tyzzer's Disease

Foals with Tyzzer's disease develop a peracute to acute multifocal necrotizing hepatitis. Grossly, hepatomegaly is evident. These foals generally have marked increases in AST and SDH concentrations. Other liver enzymes, both hepatocellular and biliary (LDH, SAP, GGT), are also increased, as are both components of bilirubin. Striking hypoglycemia should be a clue to the presence of infection with *Clostridium piliformis*. These foals often have a metabolic acidosis, with hyperlactatemia due to increased production (hypoperfusion, inflammation, catecholamine surges) and reduced hepatic clearance. Complete blood counts often reveal leukopenia with a left shift and cytologic evidence of toxicity, although leukocytosis is present in some cases.[32] Hemoconcentration reflects hypovolemia and dehydration. Hyperfibrinogenemia is common. Physical examination is consistent with septic shock, with petechial hemorrhages and injection being common. Hypovolemic shock is also evident. Mentation is usually depressed, ranging from lethargy to comatose, and icterus is a prominent finding. Clinical signs of hepatoencephalopathy may include depression, weakness, and seizures. Diarrhea is an inconsistent finding. Fever is usually present, although hypothermia from shock may be predominating when initially examined.[32]

Affected foals are often found dead. Serologic testing for recovered or suspected cases can be helpful. Pathology reveals hepatomegaly with rounded margins (Figure 11-38). Histopathologic findings with Tyzzer's disease include multifocal and random necrosis with neutrophilic inflammation (Figure 11-39). Long bacilli are often but not always seen, particularly in hepatocytes at the periphery of necrotic areas. They are best delineated with Warthin-Starry stains (Figure 11-36). An intranuclear location of the microbe has been found using electron microscopy.[33] Myocardial necrosis with Warthin-Starry stained bacilli has also been reported.[32,34] Intestinal necrosis may also be present. and organisms consistent with *C. piliformis* may occasionally be observed in sections of intestine, particularly the large intestine.[36]

Clostridium piliformis is an obligate intracellular spore-forming anaerobe. It is very difficult or nearly impossible to culture in vitro using routine microbiologic methods. Inoculation of embryonated eggs has been one means of trying to assess antimicrobial susceptibility. Penicillin, tetracycline, erythromycin, and streptomycin appear to be effective in vitro, while sulfonamides and chloramphenicol do not.[37] Treatment with dextrose, volume replacement, and sodium bicarbonate can result in temporary improvement of mentation, however most foals are reported to die.

The exact pathophysiology of infection is unknown but is believed to be oral with subsequent distribution to the liver. Ingestion of spores from feces shed by

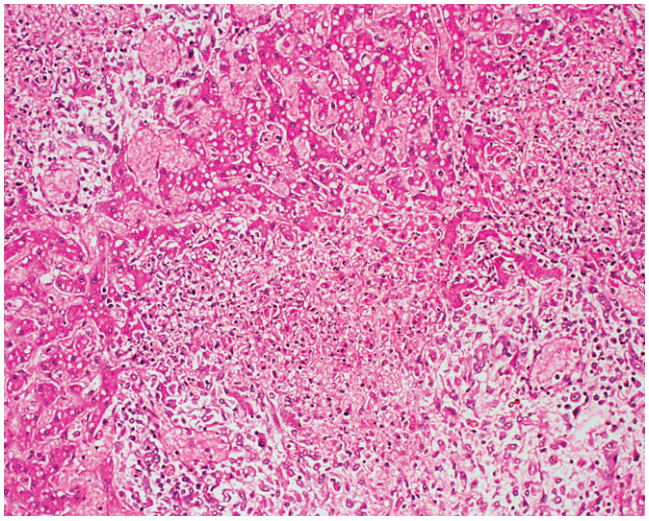

Fig. 11-39 Histopathology of a foal liver with Clostridium piliformis, Tyzzer's disease. Hematoxylin and eosin stain 10×.

subclinical carriers may play a role in development of disease, and the disease has been experimentally reproduced.[35] It has also been suspected that rabbit and rodent populations could serve as reservoirs of infection.[33] Most reported cases have been sporadic, however a number of cases have been noted on particular premises.[38] Preventive measures are unknown, however efforts should be directed at environmental hygiene on affected farms, including the use of 0.3% sodium hypochlorite to eliminate spores from barns housing affected foals.[39]

Risk factors for *Clostridium piliforme* infection in foals include foaling season, farm residency and age of mare. In one study, foals born between March 13 and April 13 were 7.2 times as likely to develop infection as those born at any other time of the foaling season.[38] Foals of nonresident visiting mares were 3.4 times as likely to develop the disease as were foals born to mares that were permanent residents of the farm. Foals born to young mares were 2.9 times as likely to develop Tyzzer's disease as those born to mares ≥6 years of age.[38]

Oxygen insufflation was administered (10 liters/minute) because of the foal's moribund state. The foal was administered Plasma-Lyte 148 and dextrose supplementation at 2% to provide 4 to 8 mg/kg/minute. The foal was administered a total of 3 liters over two hours. Once hypovolemia was corrected, the foal was administered Plasma-Lyte 56 with potassium supplementation (q 40 mEq/liter) at a maintenance rate of 4 ml/kg/hour. Parenteral nutrition (PN) was administered for nutritional support. B complex vitamins were added. Antimicrobials were continued, using a combination of ampicillin (22 mg/kg IV, q 8 h) and gentamicin (6.6 mg/kg IV, q 24 h). Seizure activity was controlled with phenobarbital. Lactulose was administered (0.1 ml/kg PO, q 8 h). Sucralfate was provided for gastric ulcer prophylaxis (20 mg/kg PO, q 8 h).

TREATMENT

Treatment of liver disease is largely supportive, with specific therapies available for certain diseases. Foals with acute hepatopathies often present in hypovolemic crises. A combination of crystalloids and colloids is indicated in volume replacement. Ideal crystalloids for liver disease include those containing acetate and/or gluconate instead of lactate, such as Plasma-Lyte 148 or Normosol-R (Abbott Laboratories, Abbott Park, IL). The liver is the primary site of lactate clearance, whereas muscle and renal metabolize acetate and gluconate is utilized by most tissues. Though accumulation of lactate from LRS does not lead to lactic acidosis (the cation associated with lactate in LRS is sodium as opposed to hydrogen ion), lactate is depressive to the myocardium; therefore iatrogenic increases in lactate concentration should be avoided. Foals with septic shock, such as those with Tyzzer's disease, should be treated with aggressive fluid therapy. Boluses of 10 to 20 ml/kg of isotonic replacement crystalloids or 3 to 5 ml/kg of colloids should be administered over 20 to 30 minutes until the hypovolemic crisis is improved or fails to improve with further volume.

If hypotension persists despite volume resuscitation, inotropes and pressors are indicated. If systemic blood pressure does not normalize in the face of a maximum or high CVP (>10 cm H_2O), dobutamine should be administered as a β-agonist inotrope (2 to 20 µg/kg/minute). Lastly, vasopressors should be administered. Norepinephrine (0.1 to 3 µg/kg/minute) or vasopressin (0.25 to 1 mU/kg/minute) can be used in an attempt to normalize blood pressure and perfusion (see Chapter 7). Oxygen insufflation (5 to 10 liters/minute) should be provided to foals with central depression, hypoventilation, or concurrent respiratory tract disease.

Because hepatic biotransformation and elimination of drugs is reduced, medications metabolized by the liver should be used judiciously and dosage alterations should be considered.

Antimicrobial therapy is indicated in cases of bacterial cholangiohepatitis or hepatitis. Broad-spectrum antimicrobials should be administered to foals with cholangiohepatitis. A combination of beta lactam, such as penicillin or ampicillin, and aminoglycoside, such as amikacin or gentamicin, is a reasonable initial choice. Ceftiofur is also a good choice, and potentiated sulfonamides can be used for long-term therapy. Foals with Tyzzer's disease may be treated with any of a

number of antimicrobials as the agent appears very susceptible to penicillin, gentamicin, tetracycline, and metronidazole.

Plasma transfusions (20 to 40 ml/kg) can be beneficial to foals with liver disease. Plasma provides additional colloid support, albumin and immunoglobulin replacement, and provision of antithrombin or clotting factors for foals with coagulopathies.

Dextrose supplementation in polyionic nonlactated fluids should be provided. Potassium chloride should be supplemented even if potassium concentrations are normal because it aids in renal excretion of ammonia. Neomycin (4 to 8 mg/kg PO, once) or metronidazole (low doses because of reduced hepatic metabolism (10 mg/kg PO q 12 h) may be administered to reduce enteric bacterial production of ammonia. Alternatively, lactulose can be used and is preferred by the author (0.1 to 0.25 ml/kg PO q 6 to 8 h).[28] Lactulose is a synthetic disaccharide that bypasses the small intestine. Fermentation in the colon results in increased nitrogen incorporation into the enteric flora, with less available for absorption. Lactulose also reduces the pH of ingesta, resulting in inhibition of ammonia generation and increased ionization of ammonia with ion trapping within the GI lumen.

For severe neurologic signs, mannitol (0.25 to 1.0 g/kg) may be administered if increased intracranial pressure is suspected. Sodium bicarbonate should not be administered unless a significant inorganic acidosis is present; rapid correction of acidemia can increase the concentration of ionized ammonia and exacerbate clinical signs. Benzodiazepines, such as diazepam, should be avoided in foals with hepatic insufficiency as they can potentiate clinical signs of hepatic encephalopathy by enhancing the effects of GABA. Seizures should be controlled with phenobarbital or pentobarbital. Flumazenil (0.5 to 1.0 mg/kg slowly IV), a benzodiazepine antagonist, can be tried in foals with clinical signs of hepatic encephalopathy that are unresponsive to other therapeutics.

Nutritional support of foals with hepatic disease is vital to a successful outcome. Parenteral nutrition should be administered to foals with fulminate hepatitis or liver dysfunction, including those with Tyzzer's disease. Formulations for patients with hepatic failure should be utilized. Protein requirements should be met but not exceeded in order to avoid contributing to hyperammonemia. Formulations with increased branch chain amino acids (valine, isoleucine, leucine) and decreased aromatic amino acids (phenylalanine, tryptophan, tyrosine, methionine) are being evaluated for use in human liver patients. Vitamin K_1 should be administered in foals with long-term liver disease. Since the liver is the primary source of vitamin C synthesis and storage of vitamins A, D, and riboflavin, a multivitamin should be provided to foals with chronic liver disease. B vitamins should be administered diluted in fluids. Vitamin E can be supplemented as an antioxidant.

Foals with portacaval shunts should be stabilized for hepatic encephalopathy, and then surgical correction can be attempted after diagnostic venography to localize the shunt.[13]

Gastric ulcer prophylaxis is indicated in select cases, particularly those with hypovolemic or hypotensive shock. Sucralfate is advantageous in that it does not undergo hepatic biotransformation. For treating ulcers, famotidine or ranitidine should be utilized, because unlike cimetidine, they are excreted primarily in the kidneys and do not inhibit hepatic metabolism of other drugs.

To everyone's surprise, '04 Jaundiced View made gradual clinical improvement over the next 24 hours. After 48 hours, her mentation improved to the point of ambulation and normal nursing behavior. The liver enzyme bilirubin and bile acid concentrations gradually decreased. The filly was discharged after 10 days with a continued course of antimicrobials for an additional week. This was a very unusual outcome for a foal with Tyzzer's disease, which is uniformly fatal.

OUTCOME

The outcome in Tyzzer's disease is generally grave. There are currently no reports of survival in documented (definitively diagnosed) cases. Some cases will improve temporarily with volume replacement and administration of dextrose and sodium bicarbonate. However, there are three reported cases and a few anecdotal reports of survival in presumptive cases of *Clostridium piliforme* infection.[38,40] Early therapy with antimicrobials and aggressive intensive care including parenteral nutrition appear to be key to a successful outcome.[40]

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