

Hemorrhagic bowel syndrome in dairy cattle: 22 cases (1997–2000)

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Objective—To determine signalment, history, and clinical, necropsy, and microbiologic findings in dairy cows with hemorrhagic bowel syndrome.

Design—Retrospective study.

Animals—22 adult dairy cows from a single farm in Colorado.

Procedure—Medical records were reviewed for information on signalment, medical and reproductive history, the owner's chief complaints, results of physical examinations and ancillary diagnostic tests, treatment and response to treatment, results of microbiologic testing, and, if applicable, postmortem findings.

Results—Common clinical signs were acute signs of profound depression, decreased milk production, tachycardia, ruminal stasis, abdominal distention, and dark clotted blood in the feces. Rectal examination revealed distended loops of small intestine in 7 of 14 cows. Transabdominal ultrasonography revealed small intestinal ileus and distention in 12 of 12 cows and homogeneous echogenic intraluminal material compatible with intraluminal hemorrhage and clot formation in 4. Seven of 8 cows treated medically died; 9 of 13 cows that underwent surgery died or were euthanized. *Clostridium perfringens* was isolated from fecal samples from 17 of 20 cows. The most common morphologic diagnosis at necropsy was severe necrohemorrhagic enteritis or jejunitis with intraluminal hemorrhage or blood clots. The most prominent histologic finding was severe, segmental submucosal hemorrhage and edema of the small intestine.

Conclusions and Clinical Relevance—Results confirm that in adult cattle, hemorrhagic bowel syndrome is a sporadic acute intestinal disorder characterized by intraluminal hemorrhage and obstruction of the small intestine. *Clostridium perfringens* was consistently isolated from the feces of affected cows. The prognosis for affected cows was grave. (*J Am Vet Med Assoc* 2002;221:686–689)

Common causes of intraluminal enteric hemorrhage in adult cattle include intussusception, volvulus, salmonellosis, bovine viral diarrhea virus infection, coccidiosis, coagulopathies, and intestinal foreign bodies. Hemorrhagic bowel syndrome (HBS) is a sporadic disorder of adult cattle characterized by acute necrohemorrhagic enteritis that primarily affects the small intestine. This disorder is distinguished from other causes of intraluminal enteric hemorrhage by the

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tendency for affected animals to develop large intraluminal blood clots that result in obstruction of single or multiple segments of small intestine. Hemorrhagic bowel syndrome has also been called fatal jejunal hemorrhage syndrome¹ and intraluminal-intramural hemorrhage of the small intestine.² Recent reports^{1,3,a-d} suggest that the frequency of this disorder may be increasing in the United States. However, little is known about the cause or typical historical, physical examination, and clinicopathologic findings. In addition, no consistent predisposing factors have been identified. The purpose of the study reported here, therefore, was to determine signalment and history of and clinical, necropsy, and microbiologic findings in dairy cows with HBS.

Criteria for Selection of Cases

Medical records of all dairy cows examined at the Colorado State University Veterinary Teaching Hospital between 1997 and 2000 because of dysentery, melena, or colic were reviewed. Records of cows with hemorrhagic enteritis were selected for additional review. Cows were considered to have HBS if they had hemorrhagic enteritis, as evidenced by melena and clotted blood in the feces or small intestine, and did not have any evidence of an intestinal or extraintestinal lesion that might cause primary obstructive disease of the small or large intestine (eg, intra-abdominal lesions, intussusception, or volvulus). Clotted blood in the small intestine was identified during transabdominal ultrasonography, an exploratory laparotomy, or necropsy.

Information regarding signalment, medical and reproductive history, and the owner's chief complaints was obtained from the medical records, along with results of physical examinations and ancillary diagnostic tests, treatment and response to treatment, results of microbiologic testing, and, if applicable, postmortem findings.

Results

Twenty-two adult lactating Holstein dairy cows from a single herd in Colorado met the criteria for inclusion in the study. Cows ranged from 2 to 8 years old (mean, 4 years; median, 4 years). Time since parturition ranged from 9 to 319 days (mean, 107.5 days; median, 100 days). Milk production records were available for 14 cows; daily milk production for these cows ranged from 72 to 158 lb of milk/d (mean, 89.9 lb/d; median, 89.5 lb/d). Data on percentage milk fat were available for 6 cows; milk fat percentage in these cows ranged from 2.5 to 5.3% (mean, 4%; median, 4%).

Eighteen of the cows were examined during 2000,

2 during 1999, 1 during 1998, and 1 during 1997. Eight cows were examined between September and November, 6 between December and February, 6 between March and May, and 2 between June and August.

Abnormalities reported by the owners at the time of initial examination included lethargy or signs of depression (n = 21), an acute reduction in milk production (8), abdominal distention (8), recumbency (5), bloody feces (2), anorexia (2), dry or scant feces (2), dehydration (2), and signs of abdominal pain, an auscultable ping, ketosis, and hypothermia (1 each).

At the time of initial examination at the teaching hospital, all 22 cows had signs of mild to moderate depression. Nineteen of the 22 (86%) cases were clinically dehydrated. Severity of dehydration was reported for 14 cows; mean degree of dehydration was 7.1% (median, 7.5%). Rectal temperature ranged from 35.1 to 39.1 C (95.2 to 102.4 F; mean, 37.9 C [100.2 F]; median, 38 C [100.4 F]). Heart rate ranged from 50 to 128 beats/min (mean, 93 beats/min; median, 96 beats/min); 13 of 21 (62%) cows had tachycardia. Respiratory rate ranged from 16 to 84 breaths/min (mean, 39 breaths/min; median, 36 breaths/min).

Ten of 17 cows were considered to have ruminal hypomotility, 10 of 17 had abdominal distention, 7 of 15 had bloody feces, and 9 of 17 had pale mucous membranes. Seven of 17 cows had an auscultable, right-sided ping; in 6 of the 7, this ping was heard in the right paralumbar fossa. Additional physical examination abnormalities included recumbency (4/17), dry or scant feces (4/17), atrial fibrillation (4/17), scleral injection (3/17), and muscle fasciculations (3/17).

Results of rectal examination were available for 14 of the 22 total cows. Four of the 14 had dark blood in the rectum, and 7 had palpably distended loops of small intestine. Other findings included a hard, firm, or large rumen (n = 4), dilatation of the cecum (2), and distention of the spiral colon (1). In 3 cows, results of rectal examination were normal.

Results of a CBC were available for 14 cows. Packed cell volumes in these 14 cows ranged from 29 to 53% (mean, 40%; median, 40%; reference range, 24 to 34%), and plasma protein concentration ranged from 6 to 9 g/dl (mean, 7.5 g/dl; median, 8.2 g/dl; reference range, 6.4 to 9.5 g/dl). Nine cows had leukocytosis, 12 had high band neutrophil counts (range, 100 to 2,400/ μ l; mean, 630/ μ l; median, 500/ μ l; reference range, 0 to 100/ μ l), and 11 had neutrophilia, with neutrophil counts ranging from 4,400 to 17,500/ μ l (reference range, 600 to 4,000/ μ l). Six cows had hyperfibrinogenemia, with serum fibrinogen concentrations ranging from 600 to 800 mg/dl (reference range, 200 to 600 mg/dl).

Results of serum biochemical testing were available for 19 cows. Eighteen of the 19 had hyperglycemia, with serum glucose concentration ranging from 105 to 550 mg/dl (median, 239 mg/dl; reference range, 55 to 95 mg/dl). Fourteen cows had hypermagnesemia; median serum magnesium concentration for these cows was 3.8 mg/dl (reference range, 1.6 to 3.2 mg/dl). Eleven cows had hyponatremia; median serum sodium concentration was 130 mEq/L (reference range,

136 to 147 mEq/L). Sixteen cows had hypokalemia; median serum potassium concentration was 3.4 mEq/L (reference range, 4 to 5 mEq/L). All 19 cows had hypochloremia; median serum chloride concentration was 82 mEq/L (reference range, 95 to 105 mEq/L). Additional abnormalities included high serum bicarbonate concentration (n = 13), high anion gap (11), azotemia (5), hypocalcemia (6), hypercalcemia (2), hyperphosphatemia (5), and hypophosphatemia (1).

Serum enzyme activities were high in several cows. Serum creatine kinase activity was high in 15 of 19 cows; median creatine kinase activity in these cows was 9,986 U/L (reference range, 57 to 280 U/L). Aspartate aminotransferase activity was high in 14 of 19 cows; median activity in these cows was 176 U/L (reference range, 40 to 130 U/L). γ -Glutamyltransferase activity was high in 13 of 19 cows; median activity in these cows was 49 U/L (reference range, 10 to 26 U/L). Sorbitol dehydrogenase activity was high in 13 of 19 cows; median activity in these cows was 58 U/L (reference range, 8 to 23 U/L).

Transabdominal ultrasonography was performed in 12 of the 22 cows. The small intestine could be imaged via the ventral aspect of the right paralumbar fossa in all 12, and dilated loops of intestine were evident in all 12 cows. In 4 cows, homogeneous echogenic material consistent with clotted blood was evident in the lumen of distended segments of intestine (Fig 1). Hypoechoic material consistent with fluid ingesta was observed in 3 cows.

Medical treatment varied. Sixteen cows were given flunixin meglumine IV shortly after admission. Thirteen cows were given fluids IV, and 7 were given fluids with electrolytes PO. Calcium salts were administered IV to 12 cows. Procaine penicillin G (22,000 U/kg [10,000 U/lb], IM) was given to 14 cows, and cefotiofur sodium (2.2 mg/kg [1 mg/lb], IM or IV) was given to 6. Additional treatments included *Clostridium perfringens* types C and D antitoxin (5 cows), nalbuphine (6), metoclopramide (5), 3% lidocaine IV (4), erythromycin (3), and oxytetracycline (3). Ancillary medical treatments included dexamethasone (2 cows), neostigmine (2), morphine (2), magnesium hydroxide

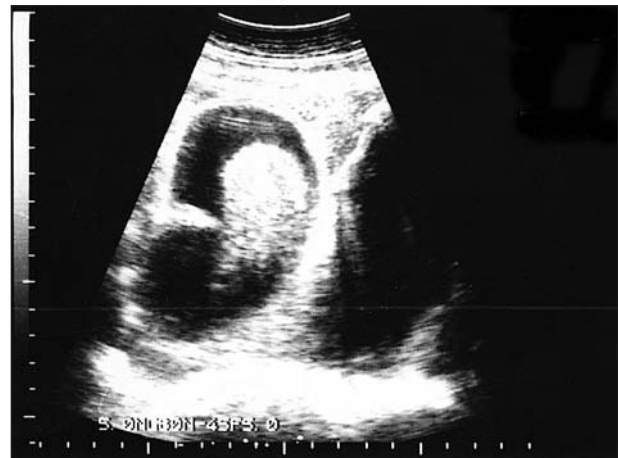


Figure 1—Ultrasonogram of the abdomen of a cow with hemorrhagic bowel syndrome. A loop of small intestine containing an intraluminal blood clot can be seen.

(2), transfaunation (2), hypertonic saline solution (2), poloxalene (1), magnesium sulfate (1), butorphanol (1), and neutral-buffered 10% formalin (1).

Eight cows received medical treatment alone, without surgical intervention; 7 of the 8 died. One cow was euthanatized prior to medical or surgical treatment. The remaining 13 cows all underwent surgery.

A right paralumbar celiotomy was performed in the 13 cows that underwent surgery. Four of the 13 were euthanatized at the time of surgery because of the severity and extent of intestinal lesions. Manual clot dissolution without an enterotomy was attempted in 2 of the remaining 9 cows, enterotomy with blood clot removal and intraluminal lavage was performed in 5, and intestinal resection and anastomosis were performed in 2. Five of these 9 cows died following surgery. Overall, therefore, 17 of the 22 (77%) cows included in the study died or were euthanatized.

The most commonly reported surgical observations in the 9 cows that recovered from surgery were hemorrhagic enteritis (9), devitalization or ischemia of the proximal portion of the small intestine, primarily the jejunum (9), distended loops of bowel (6), dark red to purple discoloration of the serosal surface of the bowel (5), and intraluminal blood clots tightly adherent to the mucosa (2). Other surgical findings included frank blood in the lumen of the intestine, sloughed intestinal mucosa, and fibrinous adhesions (1 cow each).

Biopsy specimens of the small intestine were collected from 10 of the 13 cows that underwent surgery. The most prominent histologic finding was severe, segmental submucosal hemorrhage and edema of the small intestine (9 cows). This was often accompanied by a mixed inflammatory or cellular infiltrate (8 cows). Hemorrhage and edema in the submucosa resulted in elevation of the mucosa away from the submucosa, terminating in loss of the bowel mucosa in these areas. Gram-positive rods or cocci were evident in biopsy specimens from 6 cows.

Necropsy reports were available for 12 of the 17 cows that died or were euthanatized. The most common morphologic diagnosis was severe necrohemorrhagic enteritis or jejunitis with intraluminal hemorrhage or blood clots. Several animals also had fibrinous peritonitis.

Feces from 20 of the 22 cows were submitted for anaerobic bacterial culture. *Clostridium perfringens* was isolated from 17 of the 20 (85%), with 14 of the 17 yielding moderate to heavy growth. In addition, 5 of the 10 tissue samples of affected jejunum were submitted for anaerobic bacterial culture, and all 5 yielded *C perfringens*.

Fecal samples from 15 cows were submitted for aerobic bacterial culture for salmonellae, fecal samples from 6 cows were submitted for fluorescent antibody testing for bovine viral diarrhoea virus, fecal samples from 4 cows were submitted for a polymerase chain reaction assay for epizootic hemorrhagic disease virus, and fecal samples from 2 cows were submitted for a polymerase chain reaction assay for bluetongue virus. Results for all of these tests were negative, except that *Salmonella* spp was isolated from 1 cow from which *C perfringens* was isolated.

Ten of the 17 *C perfringens* isolates were genotyped with a multiplex polymerase chain reaction assay. For each isolate, 4 to 6 individual colonies were selected on the basis of colony characteristics consistent with *C perfringens* colony morphology and a double zone of hemolysis on blood agar plates. Five of the 10 isolates from cows with HBS were identified as *C perfringens* type A, and 5 were identified as *C perfringens* type A with the $\beta 2$ toxin gene. Four of the 5 cows from which *C perfringens* type A was isolated died, whereas all 5 cows from which *C perfringens* type A with the $\beta 2$ toxin gene was isolated died.

Discussion

Results of the present study confirm previous reports that HBS is a sporadic acute intestinal disorder of adult cattle characterized by intraluminal hemorrhage and obstruction of the small intestine. Medical treatment of HBS was largely unsuccessful in these cows, with 7 of 8 cows treated medically dying. Surgical treatment was slightly more successful, but 9 of 13 cows that underwent surgery died or were euthanatized. However, 4 of 9 cows in which the obstruction could be removed at the time of surgery or in which the affected segments of intestine could be resected survived. Although a definitive cause was not identified in these cows, *C perfringens* was isolated from feces from 17 of 20 cows.

Although various names have been coined for this syndrome, the term HBS was chosen for the present study as being the most descriptive. Other names that have been used suggest that the disease is invariably fatal (eg, fatal jejunal hemorrhage syndrome³), which was not the case for cows in the present study, that the disease is localized to jejunum (eg, jejunal hemorrhage syndrome¹), or that intraluminal bleeding is the predominant disease process (eg, intraluminal-intramural hemorrhage of the intestine²). In our opinion, reference to this condition as a syndrome better implies the lack of knowledge regarding etiology.

Hematologic and serum biochemical abnormalities among cows in the present study were largely reflective of the acute nature of HBS and the resultant gastrointestinal stasis. Neutrophilia with an accompanying increase in segmented neutrophil count may be attributable to release of inflammatory cytokines, leading to subsequent release of neutrophils from the bone marrow. Alternatively, high neutrophil counts may be attributable, at least in part, to endogenous steroid release associated with the stress of disease.^{4,5} Similarly, hyperglycemia may be attributable to the stress of disease, with resultant endogenous steroid and epinephrine release. Functional or physical obstruction of the proximal portion of the small intestine in these cows likely resulted in sequestration of abomasal secretions, with resultant hypochloremia and hypokalemia. Increases in enzyme activities, particularly activities of sorbitol dehydrogenase, aspartate aminotransferase, and γ -glutamyltransferase, were most likely a result of acute liver damage associated with gastrointestinal obstruction or stasis and absorption of bacteria and toxins from areas of intestinal damage.⁴ The increase in creatine kinase activity was likely indicative of muscu-

loskeletal damage associated with systemic disease and myodegeneration associated with recumbency.⁴

Risk factors for HBS have not been identified, and the present study was not specifically designed to identify risk factors. However, 14 of the 22 (64%) cows in the present study developed HBS during the first 3 months after parturition. Stress associated with high-intensity milk production, increased energy in the ration, and decreased fiber in the diet have been proposed as risk factors for development of this syndrome.^{2,3}

Although a definitive cause of HBS in cattle has not been identified, several reports^{1-3,5-7,a} have indicated an association between *C perfringens* type A and HBS. In the present study, *C perfringens* was isolated from 17 of 20 fecal samples and from 5 of 5 intestinal biopsy specimens. However, the organism is presumed to be a part of the normal flora of the intestine of livestock^{6,8} and proliferates quickly after death, making results of bacterial culture of fecal samples of questionable diagnostic importance.^{1,6,9-11,a} In addition, *C perfringens* is ubiquitous in the environment and is a commensal organism in the gastrointestinal tract of most mammals.^{7,9,12,13} Thus, it is unclear whether proliferation of *C perfringens* is part of the primary disease process in cows with HBS or occurs as a secondary response. However, *C perfringens* type A has been isolated from intraluminal blood clots obtained from the jejunum at the time of surgery or necropsy in cattle with HBS.^{b-d} In addition, in regions of affected bowel, there is histologic evidence of intestinal necrosis with intraluminal growth of large, gram-positive, rod-shaped bacteria.^{b-d} Thus, we believe that *C perfringens* may be important in the pathogenesis of this syndrome.

Although clinical and histologic findings for cows in the present study with HBS were similar to findings reported for other species with clostridial enteritis,^{2,7} intraluminal bleeding with subsequent development of large adherent clots was a consistent finding in these cows. Such intraluminal bleeding is not typically associated with clostridial enteritis in other species, and the cause of clot formation in cows with HBS remains unclear at this time.

A multiplex polymerase chain reaction assay^{14,15} was used to genotype *C perfringens* isolates from 10 cows in the present study. Five of the isolates were *C perfringens* type A, and the other 5 were *C perfringens* type A with the $\beta 2$ toxin gene. Currently, however, no vaccine approved for use in cattle in the United States contains *C perfringens* type A or *C perfringens* type A with the $\beta 2$ toxin gene. Bacterin-toxoids for types C and D are currently available but do not appear to protect cattle from HBS.^{1,6} The dairy from which all cows

in the present study came routinely vaccinated all animals 2 or 3 times a year with a *C perfringens* types C and D toxoid.

^aMaddox C, Hattel A, Drake T, et al. *Clostridium perfringens* type A strains recovered from acute hemorrhagic enteritis of adult lactating dairy cattle (abstr), in *Proceedings*. Annu Meet Am Assoc Vet Lab Diagn 2000.

^bDennison A, Callan R, VanMetre D, et al. Retrospective analysis and clinical investigation of hemorrhagic bowel syndrome in adult dairy cattle (abstr), in *Proceedings*. 81st Annu Conf Res Workers Anim Dis 2000.

^cDennison A, VanMetre D, Callan R, et al. Hemorrhagic enteritis of adult cattle (abstr), in *Proceedings*. 19th Annu Vet Med Forum 2001;354.

^dDennison A, Plampin E, Magnuson R, et al. PCR, ELISA and lecithinase activity assays as tools for determining the significance of *C perfringens* in HBS of adult cattle (abstr), in *Proceedings*. 2001 Colo State Univ Integrated Livestock Manage Forum 2001.

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