

Hemorrhagic Bowel Syndrome

Investigators:

Dave Van Metre DVM, PhD, ACVIM, Dip
Rob Callan DVM, PhD, ACVIM, Dip

General Project Area Description:

Hemorrhagic Bowel Syndrome (HBS) is a newly emerging, highly fatal intestinal disease of adult dairy cows in the United States. This disease has also been called Jejunal Hemorrhage Syndrome, bloody gut, or clostridial enteritis. The disease is seen most commonly in adult dairy cows early in lactation, although cases occasionally occur in late lactation or the dry period. It commonly occurs as an occasional disease on most dairies, although several cows may be affected in a relatively short period of time, and some dairies struggle with this disease on virtually a continual basis. Affected cows are rapidly debilitated by the combined effects of sudden and massive hemorrhage into the small intestine. As a result, affected cows may simply be found dead or dying. The cow's extremities are often cool and the rectal temperature is often subnormal, reflecting the loss of blood into the intestine and the resulting shock. The feces of affected cows is dark, tar-like, and may contain dark red to black clots of digested blood. As clots form in the affected segments of the intestine, the intestine may become obstructed, causing some cows to become bloated and show signs of colic. The affected segments of intestine quickly die and will occasionally rupture, resulting in invariably fatal peritonitis. Successful treatment of this disease is difficult. Occasional anecdotal reports exist of successful treatment with fluids, laxatives, anti-inflammatory drugs, and antibiotics; however, it appears that such treatment successes are quite rare. More frequently, if treatment is attempted, the veterinarian will perform abdominal surgery and attempt to either break down the clots in the affected segments or remove the segments of damaged and obstructed bowel. Reports to date indicate that the prognosis for successful surgical treatment can vary extensively. Unfortunately, in our experience, surgical treatment is usually not successful, because affected cows can develop repeated clotting and recurrent obstruction of the intestine after surgery. Also, in many cases, multiple segments of the intestine are obstructed with clots and nonviable by the time surgery occurs, making removal of affected intestine impossible. In addition, some affected cows have developed severe peritonitis by the time of surgery and must be euthanized. Of 22 cows affected with HBS presented to our clinic over a 3-year period, only 6 (27%) survived.

What is the cause of HBS? The cause of HBS is currently unknown, and no consistent predisposing factor has been identified. While infectious agents such as bovine viral diarrhea (BVD) virus and Salmonella may cause bloody diarrhea in affected cows, the symptoms, disease course, and necropsy findings are dramatically different from HBS. The majority of HBS cases seen at the VTH occur during the first 3 months postpartum. The physiologic stress associated with peak milk yield may therefore be involved, as well as the relatively high-energy, low-fiber rations fed during this stage of production. We have been unable to definitively link HBS to a particular feed component in the dairies

that we service. Cases have occurred during all times of the year, although we tend to see more cases in the fall and winter months.

Is there an association between *Clostridium perfringens* type A and HBS? Several reports indicate an association between *Clostridium perfringens* type A and HBS. This association is based on the following observations:

- (1) Affected cows often have positive fecal cultures for this organism.
- (2) *C. perfringens* type A can be readily isolated from intraluminal blood clots in the jejunum of affected cows.
- (3) There is microscopic evidence of intestinal wall damage associated with heavy growth of *C. perfringens* type A.
- (4) Other infectious agents associated with hemorrhagic enteritis are rarely identified in tissues or enteric contents of affected cows.

What is *Clostridium perfringens* type A? *Clostridium perfringens* type A is a bacteria that is considered to be widespread in the environment and in the gastrointestinal tract of most mammals. Interestingly, previous research has shown that the rate of isolation of this organism from the gastrointestinal tract of cattle may be enhanced by high grain diets. An important fact to know is that this organism proliferates rapidly in the intestine of most cattle after death, making isolation of *C. perfringens* type A from decomposed carcasses of questionable diagnostic significance.

Is *Clostridium perfringens* type A a primary or secondary factor in HBS? It is unclear at present whether enteric proliferation of, and intraluminal toxin production by *C. perfringens* type A occurs as part of the primary insult to the intestine, or if these processes occur secondary to another disease or triggering factor. Hemorrhage into the intestine from another cause could, in theory, initiate secondary proliferation of the ubiquitous *C. perfringens*, as this organism is likely to rapidly multiply when large quantities of soluble protein or carbohydrate is presented to the intestine. In other words, blood certainly could act as a very rich culture medium for this organism. Once the organism proliferates, however, the toxins that it releases during rapid growth could contribute to the degradation of the intestinal wall that is so characteristic of HBS. This destruction of the intestinal wall in sections of the gut affected by HBS is likely to contribute to the subsequent shock and peritonitis that is evident in so many affected cows.

What about the the role of *Aspergillus fumigatus* in HBS? Investigators at Oregon State University have focused on characterizing the role of *Aspergillus fumigatus*, a mold (fungus) that can be found in livestock feeds. Genetic material of this fungal agent can be detected in the blood and intestine of affected cattle. A research project involving dairy cows with HBS and dairy cows that have died of other gastrointestinal diseases (the control group) is currently being conducted by investigators in Wisconsin, Minnesota, and Oregon.³¹ In this study, the rates of isolation of *C. perfringens*, *Salmonella*, and bovine viral diarrhea virus are being compared among cows of these two groups. In addition, the rate of detection of *Aspergillus fumigatus* DNA by polymerase chain reaction in the tissues is being compared among cows of the two groups. Statistical

analysis of preliminary data has revealed a significant association between HBS and the presence of *A. fumigatus* DNA in the tissues. In other words, the DNA of this fungal organism was present in the tissues of a significantly greater proportion of cows with HBS than of cows that died of another GI disease. However, because *C. perfringens* type A was isolated from cows of both groups, no statistical disparity was found among the two study groups for the presence of *C. perfringens*, although the authors indicated that future data may produce different results on this issue.

There are currently two hypotheses regarding the participation of *A. fumigatus* in this disease:

(1) As a primary contributor to the intestinal lesion.

or

(2) As an agent that impairs the cow's immune system, thereby facilitating or inciting whatever disease process triggers HBS. Anecdotal reports suggest that the incidence of HBS can be reduced on dairies following the introduction of a feed supplement (Omnigen AF®) into the ration. Controlled studies on the efficacy of this product for HBS prevention are pending. This product has recently been demonstrated to improve certain indicators of immune function in the white blood cells taken from immunosuppressed sheep and cattle.

Research:

Completed studies

2001-2002 Hemorrhagic bowel syndrome in dairy cattle: A pilot study to determine the role of *Clostridium perfringens* type A. PI: Van Metre DC. CRC Experiment Station Grant, \$26,000.

2002-2003 Hemorrhagic bowel syndrome of dairy cattle: Continued investigation to determine the role of *Clostridium perfringens* type A. PI: Van Metre DC. CRC Experiment Station Grant, \$10,000.

2002-2/03) Hemorrhagic bowel syndrome of dairy cattle: Continued investigation to determine the role of *Clostridium perfringens* type A. Animal Population Health Institute, Colorado State University / USDA: CSREES, \$10,000.

Future Proposed Studies:

1. Evaluation of the effect of bovine blood on alpha toxin production by *Clostridium perfringens* type A.
2. Evaluation of the effect of *Aspergillus fumigatus* on toxin production and toxin gene transcription by *Clostridium perfringens* type A.

Publications:

Abstracts:

Dennison A, Plampin E, Ellis R, Van Metre D, et al (2001). Correlation of *Clostridium perfringens* a toxin activity and disease severity in isolates from cows with hemorrhagic

bowel syndrome (abstract). Proceedings, 82nd Annual Meeting, Conference of Research Workers in Animal Diseases, 108.

Dennison A, Van Metre D, Callan R, Mason G, et al (2002). Hemorrhagic bowel syndrome of adult cattle; A comparative investigation to determine the role of *Clostridium perfringens* Type A (abstract). Proceedings, Conference of Research Workers in Animal Diseases, Chicago, IL, 110.

McKay JT, Ellis RP, Dennison A, Morley PS, Van Metre DC (2004). Comparison of alpha toxin activity between *Clostridium perfringens* isolates from cattle affected with hemorrhagic bowel syndrome (HBS) and left displaced abomasum (LDA). Proceedings of the 85th Annual Meeting of the Conference of Research Workers in Animal Diseases, Chicago, IL, Abstract 115.

Van Metre D, Callan R, Morley P, et al. (2004). Comparison of the rate of isolation, genotype, and in vivo toxin production of *Clostridium perfringens* from the gastrointestinal tract of dairy cows with hemorrhagic bowel syndrome and herd mates with left displaced abomasums. Proceedings, 23rd World Buiatrics Congress, 115.

Referred Articles:

Dennison AC, Van Metre DC, Dinsmore RP, et al. Hemorrhagic bowel syndrome of adult dairy cattle: 22 cases (1997-2000). *Journal of the American Veterinary Medical Association*, 221:686-689, 2002.

Berghaus; McCluskey; Callan. Risk factors associated with hemorrhagic bowel syndrome in dairy cattle. (*Journal of the American Veterinary Medical Association*. 2005 May 15; 226: 1700-6.

Dennison AC ; Van Metre DC ; Morley PS ; Callan RJ ; Plampin EC ; Ellis RP. Comparison of the odds of isolation, genotypes, and in vivo production of major toxins by *Clostridium perfringens* obtained from the gastrointestinal tract of dairy cows with hemorrhagic bowel syndrome or left-displaced abomasum. *Journal of the American Veterinary Medical Association*. 2005 Jul 1; 227(1): 132-8.