HOST, PATHOGEN, AND ENVIRONMENTAL INTERACTIONS RESULTING IN HEMORRHAGIC JEJUNAL SYNDROME IN DAIRY CATTLE

Bill Seglar, DVM, PAS
Global Nutritional Sciences Manager
Pioneer Hi-Bred Intl., Inc.
Box 1150
Johnston, IA 50131-1150

Introduction

Dynamic digestion kinetic interactions along with presence of gastrointestinal pathogens in dairy cattle may result in the formation of disease complexes. Sporadic observations of dairy cows succumbing to acute death due to a syndrome known as hemorrhagic jejunal syndrome (HJS) is one such example. North American dairy veterinarians have reported the syndrome, also known as hemorrhagic bowel syndrome (HBS), hemorrhagic enteritis, or Clostridial enterotoxemia, with increased incidences in recent years.

The prevalence of HJS in the Midwest during the 1970s-1980s was an occasional diagnosis made by veterinarians who usually blamed the syndrome onto overeating disease. Basically cows housed in traditional stanchion barns were fed legume/grass hay forages with minimal silage and batch fed ground feed mix. Veterinary explanation was that cows sorted out fiber and over consumed ground feed mixes, resulting in classical symptoms of Clostridial related enterotoxemia. However, incidences of the syndrome dramatically increased as Midwest dairy producers transitioned into modern free-stall facilities that often involved all silage forages with no dry hay, total mixed rations (TMR), tighter forage to concentrate ratios, and higher production expectations.

Based on practitioner and producer reports from NE Iowa, SE Minnesota and SW Wisconsin, as well as reports from across the nation during 1999, clinicians at Iowa State University suspect that Hemorrhagic Jejunal Syndrome (HJS) is possibly a new emerging disease syndrome. Presentation of this disease has been sporadic in morbidity: presenting on individual dairies and affecting individual mature cows. A morbidity of 1-2% of the mature cow population could be expected on affected dairies based on practitioner reports. Mortality of affected

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animals will approach 85-100% due to the peracute nature and severity of this disease [2].

Clinical Signs and Post Mortem Findings

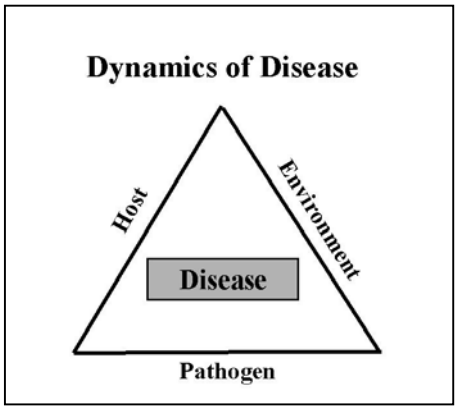
HJS can be characterized as being peracute. Frequently the producer will see no prodromal signs and witness a sudden death, or an individual that is down and in systemic collapse. Clinical signs include:

- Sternal recumbency
- Vocalization of pain
- Sweats
- Bruxism
- Sunken eyes from dehydration and pain
- Shock – pale mucous membranes and cold clammy ears
- Ballotment of the standing cow in the lower right abdomen can elicit a pronounced fluid slosh due to the backup of ingesta and fluid behind the occlusive lesion.
- Rectal examination may show signs of constipation, followed by evidence of melena or frank hemorrhages and clots within the rectal vault. Dilated gut loops may also be palpable.

Veterinary post-mortem observations demonstrate consistent segmental lesions in the jejunum vs. diffuse whole tract involvement. These areas consist of frank hemorrhage (diapedesis) and immediate clotting forming a functional occlusion of the lumen of the small intestine. Necrosis of the lumen may or may not be apparent. Some cases have also presented intussusceptions in addition to the areas of hemorrhage and clotting. This lesion could be suggestive of hypo- or hyper-motility that would result in the slowing of ingesta flow allowing Clostridial growth and sporulation [2].

Etiology of HJS

Some nutritionists and veterinarians speculate that an association exists between HJS and the feeding of Clostridial silages to dairy cattle. The likelihood of disease occurring is more detailed than the mere presence of a pathogen in a feedstuff. Three dynamic conditions must exist for a disease to occur: 1) presence of the pathogen, 2) presence of a host, and 3)



favorable environmental conditions for proliferation of the disease [7]. In completing the first part of the triangle, pathogenic Clostridial organism may come from silage, any other feed, or from non-feed sources on the farm since the microbe is a naturally occurring soilborne microorganism, which is ubiquitous and can be found as a part of the gut flora of warm-blooded animals [1]. Clostridial organisms as well as many other microbes go through cattle digestive tracts everyday with no problem, however the disease will result if the host (the cow) and the environment (lower intestinal tract) are set up to allow proliferation *Cl. perfringens* and allow toxin production.

The Pathogen:

Veterinary diagnostic laboratories usually diagnose type-A toxin as the cause of HJS. There exists 5 phenotypes that are classified as types A,B,C,D, and E. Each phenotype produces 4 major endotoxins known as α, β, ε, and ι, although many other unidentified toxins may exist. However, the most common agent causing HJS in dairy cattle is *Clostridium perfringens* type A and usually is associated with the production of α toxin [10]

Clostridial perfringens is one of the Clostridial organisms that can be isolated in silage. Veterinarians findings also indicate the microbe exists in other feedstuffs also, such as steam flaked corn in Colorado and soybean meal in Ohio. The table below is a classification of Clostridial organisms found in silage [3,12].

Saccharolytic	**Proteolytic**	**Others**
C. butyricum	*C. bifermentans*	*C. perfringens*
C. paraputrificum	*C. sporogens*	*C. sphenoides*
C. sphnoides	*C. botulinum (type B)*	
C. tyrobutyricum		
C. scatol (rare)		

Soil coming in with crops (as a result of muddy harvest conditions, harvest implements digging into soil, and wind) acts as a vector for soilborne Clostridial organisms being present in feedstuffs. Heavy manure applications on fields where minimal tillage practices exist may exacerbate the Clostridial spore loads on crops. Various amounts of soil are always harvested with the crop depending upon weather conditions and dictate the epiphytic populations and diversity of microbial spores coming in with the crop. Ash is an analytical measure that can be used to assess how much soil was incorporated with the crop after adjusting for major macro-minerals. For instance, an alfalfa sample with 12% ash has 1.5% calcium, 0.3% phosphorus, 0.3% magnesium, and 3% potassium, which add up to a 5.1% contribution from macro-minerals. One might speculate that an additional

1% comes from trace-minerals for a total mineral content of 6.1%. This means that 5.9% of the alfalfa ash is composed of soil minerals. The average ash level is 11.5% for alfalfa samples submitted to the Pioneer Technical Service system. Therefore the sample used in this example is about average for the amount of soil ensiled with the crop.

Silages displaying indications of Clostridial fermentation (high pH, high moisture, presence of butyric acid and elevated ammonia nitrogen) do not verify that *C. perfringens* exists in silage. A small-scale study using 31-corn and alfalfa silage samples from Pioneer technical services were submitted to University of Arizona's Clostridial enterotoxemia laboratory to determine if *C. perfringens* Type A α toxin was present [(9)]. Silage analysis of the 31samples revealed that 10 of the silages had elevated butyric acid and ammonia nitrogen levels while the other 21 were normal. The Arizona laboratory found *C. perfringens*, Type A present in 3 samples that were considered normal and well-fermented silages. Conversely, those silages diagnosed as Clostridial silages by Pioneer Technical Services failed to display the presence of the *C. perfringens* toxin. These findings indicate that well preserved silages may harbor *C. perfringens,* but yet not cause enterotoxemia symptoms within the herd.

The Host:

Dairy cows affected by HJS usually have a history of being high production animals with high dry matter intakes. The dairy may have TMR mixing inconsistencies resulting in less than required fiber and effective fiber intakes, resulting in excessive amounts of concentrate rations being delivered to the cow. Cows may be sorting the TMR mix, where a properly mixed ration is delivered to the cows, but they end up consuming a ration that is low in fiber and high in concentrate. Sub-acute ruminal acidosis may be a predisposing health condition in he herd. High carbohydrate levels, or low fiber levels may predispose lactating cows to subclinical ruminal acidosis defined by a rumen pH of < 5.5. Suspect pH readings are 5.8 or less [(5)].

Milk production potential of dairy cows may be associated with the likelihood of HJS to occur at a dairy operation. An Iowa State Veterinary College case study indicates a trend with increases in management level milk and an increase in death losses [(2)]. The increased production of milk could be identified as a potential risk factor in the presentation of HJS. Furthermore milk production can be broken down into sub-categories of risk.

- The first sub-category - presentation of starch (energy). Milk production is related to the presentation of carbohydrates in the form of grain and if the

energy density of the consumed ration is high it may predispose the affected cow to ruminal acidosis. The presence of energy dense rations may represent a further risk through predisposition of the animal to intestinal Clostridial growth and sporulation.

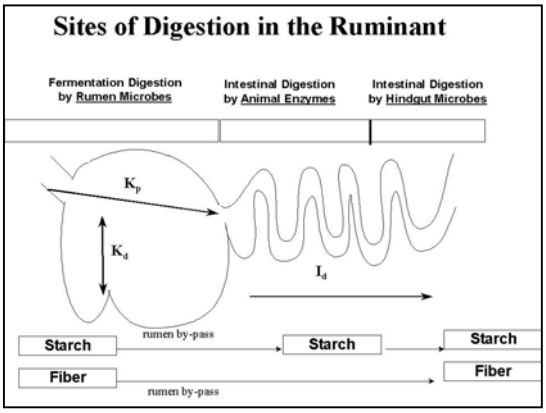
- The second sub-category of risk is related to dry matter intake by the cow. Milk production follows energy intake, which follows feed intake. Dry matter intake may be a risk factor due to starch consumption levels, or due to some as yet undescribed decrease in intestinal motility related to high ruminal fill rates.
- The third sub-category on this particular dairy is alfalfa silage consumption. Removal of this product due to a shortage following the field investigation yielded an immediate 5-lb decrease in milk per cow. One month later the product became available with the result that milk production rebounded the lost 5 lb.

Kirkpatrick at Iowa State found that primiparous cows had lower overall dry matter consumption and greater milk production persistency than multiparous herd mates. There appeared to be no association between the early milk production of the first lactation individuals when compared to the death loss. Conversely, the multiparous individuals showed increases in milk production that corresponded to the increases in death losses. In this investigation, there were no deaths in the first calf heifers. The explanation for this phenomenon could be that primiparous cows had a lower dry matter intake than multiparous cows.

Another host related factor that could contribute to HJS is the presence of mycotoxins in dairy rations. Scientific evidence is lacking if commonly diagnosed vomitoxin causes problems in dairy cattle. However, recent research at Minnesota show that patulin, a Penicillium-produced mycotoxin can have inhibitory microbial effects on the rumen [8].

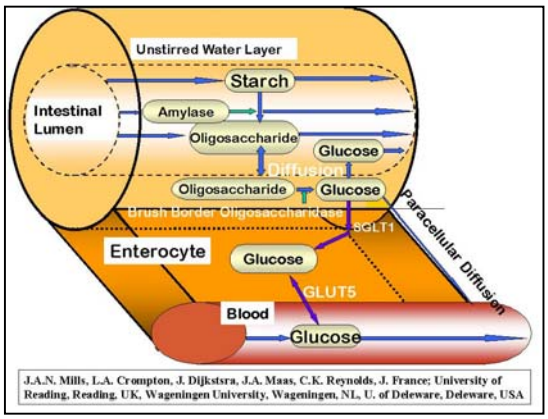
The Environment:

The environmental leg of the disease triangle determines if conditions exist for Clostridial proliferation in the lower intestinal tract. For purposes of discussion, this section of the digestive tract can be called the hindgut. As indicated by the illustration on the right, digestion kinetics dictate the sites where nutrients are fermented or digested in the ruminant's digestive



tract. The rate of digestion (K_d) and rate of passage (K_p) determine how much starch and fiber is fermented within the rumen. Once fiber leaves the rumen, hindgut microbes will continue to ferment fiber, however the microbial protein that is produced is lost into manure and minimal amounts of volatile fatty acids are absorbed by the cow. Starch leaving the rumen continues to be degraded into glucose by intestinal enzymes (I_d). Remaining starch entering the hindgut may then undergo further fermentation.

Considerable quantities of starch escape rumen fermentation when high yielding dairy cows are fed energy dense diets. Limitations to enzyme activity and glucose transport activity along the small intestine may lead to inefficient dietary energy retention. Therefore, a dynamic mechanistic model was constructed by the collaboration of researchers from the University of Reading, University of Delaware, and Wageningen University, to investigate the flow and degradation of starch and the transport of glucose in the small intestine for dairy cows fed a range of nutrient intakes [4]. Limitations to individual metabolic processes, particularly to starch digestion in the proximal region of the intestine can create asynchrony between starch degradation and glucose uptake capacity.



The model demonstrates that the amount of substrate reaching the hindgut is dependant upon 7 several variables: 1) starch, 2) glucose, 3) enzymatic activity, 4) the intestinal lumen, 5) the unstirred water layer, 6) the enterocyte and 7) blood. Each pool is represented by a differential equation. The model describes 1mm of intestinal length and is repeated for each meter of the intestine, with outputs from one section forming inputs to the next. Model simulations indicate that as duodenal starch increases, there exists increased glucose and oligosaccharide flow in the lower intestinal tract. The model also indicates that as duodenal pH decreases, the amount of starch flow is increased in the lower intestinal tract. One may speculate that the presence of increased substrate to the hindgut for microbial proliferation may cause the hindgut pH to change and create a suitable environment for Clostridial activity.

Research findings regarding the effects of pancreatic amylase production and changes in osmolality can be used to speculate how a desirable environment is achieved in the hindgut for Clostridial proliferation. For instance, early University of Kentucky work suggests that protein in the diet determines how much pancreatic amylase will be produced for starch digestion [13]. However in a recent paper delivered at the 2001 ASAS/ASDS/PSA meetings, researchers at University of Kentucky showed that starch masks the effect of protein (casein) and that starch is the dominant controller of amylase secretion and that protein will only stimulate amylase when starch levels are lower [11]. This leads to speculation of the effect of excessive starch and/or glucose reaching the hindgut.

Research observations from Dr. Fred Owens suggests that ample amylase is present for starch degradation, but that visual clues suggest that particle size and grain exposure rather than enzyme deficiency determine the extent of starch digestion by either microbes or intestinal enzymes [6]. Dr. Owens suggests that high osmotic pressure may explain why additional substrate might reach the hindgut. One might assume that with high osmolality in the rumen, digesta with high osmolality is pushed into the intestines and has similar effects there. Such digesta, if present in the small intestine, probably would cause mucosa of the intestines to become edematous with tissue fluids. Some studies with lambs from Nebraska suggest that following a bout of acidosis, absorption from the small intestine is reduced as long as a month after a bout of acidosis.

Summary

After reviewing the many dynamic pathogen, host, and environmental interactions that may contribute to the onset of HJS, a conclusion can be drawn that there is more involved than the mere ingestion of Clostridial silages by dairy cattle. Excessive starch and /or sugar levels reaching the hindgut may result in changes in the environment of the hindgut that results in altering of pH and permitting Clostridial organisms to proliferate. HJS may result when favorable conditions exist for the three legs of the disease triangle.

Controlling the syndrome involves monitoring several aspects of the dairy operation.

- Monitor for TMR mixing inconsistencies using the Penn State Particle Separator on total mixed rations and forages. Particle separation measurements should be been taken of the forages going into the total mixed ration (TMR) and then particle separation measurements taken to

determine course screen retention of the final TMR. Additionally, refusals should be analyzed for course particle refusals to determine if sorting is occurring. If sorting is occurring or course particles are lacking from TMR mixing, then this would contribute to likelihood of cows to develop HJS.

- Note any major feeding changes occurred in dairy operations in the past 1-2 years. Energy densities in rations should be compared to determine if they are higher now than in prior years. Observe if non-fiber carbohydrate (NFC) levels are approaching or greater than 40% in the ration. Observe if dairy herds are transitioning from dry hay forage systems to an ensiled forage system.

- Are dry matter intakes higher than in the past? Higher production cows will have higher dry matter intakes, and if rumen problems are an issue, it's easier for these cows to develop HJS than ones with lower dry matter intakes.

- Examine the TMR for nutrient composition using wet chemistry analysis to assure the ration formulated on the computer is the same as what's being offered to the cow.

- Have the affected dairies had other herd problems such as increased incidences of sole abscesses being corrected by the hoof trimmer? If so, this would suggest rumen acidosis might be a factor explaining why HJS is breaking.

- Monitor the herd and individual cow butterfat tests and determine if excessive fat:protein inversions exist. A dairy herd with more than 10% fat:protein inversions may have sub-acute ruminal acidosis which could predispose HJS.

- Monitor blood calcium levels at parturition. Cows freshening with slightly lower than average calcium can exhibit hypo-motility of the rumen and preclude HJS. In addition too much potassium in the blood (hyperkalemia) could tie up magnesium (hypomagnesia) resulting in a syndrome similar to not having enough calcium resulting in rumen stasis [(2)]. Transition cow management should be monitored if low calcium or high potassium blood levels exist.

- Minimizing the amount of soil coming in with the crop to lessen numbers of pathogenic spores. Avoid over-application of manure applications and correctly time slurry applications. Follow good harvest management practices and use a research proven forage additive to ensure optimum fermentation of the crop.

- Analyze ensiled forages for fermentation. Several commercial laboratories now offer fermentation-testing services that can examine silages for pH, silage acid composition, and ammonia nitrogen levels to determine if poor fermentation has predisposed the silage to Clostridial fermentation.

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