Pathophysiology of Lower Gastrointestinal Tract Problems in the Bovine

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Introduction

The problems of the lower gastrointestinal tract in the cow can be divided into two major categories: (1) diarrhea, and (2) obstruction with lack of adequate fecal output. Less common problems would include bleeding in the intestinal tract, tenesmus or straining, and pain in the abdomen.

Diarrhea is the most prominent problem of the gastrointestinal tract facing the large animal practitioner of today. In fact, diarrhea or the complications associated with diarrhea account for 10-15% of the mortality losses associated with calves born in the United States! Some data indicate this is the major loss to the cattle industry in the United States.

What is diarrhea? Diarrhea as defined early by Hippocrates is the abnormal frequency and liquidity of fecal discharges (2). Certainly, this definition applies today regardless of species. However, the frequency of defecation varies with the species, diet and even the season of the year, as the cow out on pasture in the summer has more frequent fecal discharges than does the cow during the stabling season.

Once diarrhea has been defined, we must consider the pathophysiological mechanisms producing diarrhea. These can be listed in five major headings: (1) *osmotic material* in the gastrointestinal tract, (2) *secretory diarrhea,* (3) *inhibited absorption,* (4) changes in *mucosal permeability,* and (5) *deranged motility* (3).

1. Osmotic material in the gastrointestinal tract can be further classified in three subdivisions.

A. *Poorly absorbed solutes* would include osmotically active solutes like magnesium sulfate and magnesium oxide, which are common saline laxatives used by practitioners today and used primarily for the purpose of causing diarrhea.

B. *Maldigestion* is another possible cause of osmotic diarrhea, however, it is rarely recognized in large animals. Maldigestion can be associated with pancreatic deficiency in the dog, specifically, pancreatic atrophy or hypoplasia in the young German shepherd or maldigestion following pancreatic fibrosis in older dogs (4,5).

C. Osmotic diarrhea is the third cause of solute transport failure. In this situation, material that is normally absorbed in the intestinal tract is not absorbed because of an enzymatic defect in the mucosal cells. The best example of this would be sucrose or common table sugar. Calves cannot absorb sucrose as it must be hydrolyzed in the gut by the enzyme sucrase in the intestinal mucosa; calves lack the enzyme sucrase (6,7). Sucrose present in the diet of a young calf will act as an osmotic agent to cause diarrhea. Hence, we should emphasize to owners they should *not* use table sugar for nutrient supplementation in young calves.

2. *Secretory diarrhea* can be broken down into several categories.

A. *Passive secretion* of electrolytes across the intestinal mucosa into the lumen of the bowel. This category can be broken down into two subtypes of disease processes: inflammatory diseases and non-inflammatory diseases. As we review the absorptive process, we can appreciate that nutrients, electrolytes and water are constantly being absorbed from the luminal side of the bowel through the villi and into the bloodstream and at the same time there is continual secretion of water and electrolytes from the bloodstream through the villi into the lumen of the bowel, establishing a bidirectional flux across the intestinal mucosa.

Examples of inflammatory diseases associated with increased passive secretion would include salmonellosis (8), bovine virus diarrhea (9), Johne's disease (10,11), and invasive *Escherichia coli* (12,13). Non-inflammatory diseases would include heart failure, lymphosarcoma (14), posterior vena caval obstruction, and amyloidosis (15). It may not be apparent why amyloidosis should be associated with diarrhea. It is due to the renal loss of protein, specifically, albumin, which results in a prominent hypoproteinemia. The plasma concentration of protein becomes so low to lower the oncotic pressure of the plasma, therefore, the electrolytes are not efficiently absorbed across the intestinal tract.

Johne's disease has several mechanisms to produce diarrhea but at least one of these is increased passive secretion, and, whenever we see a debilitated animal with chronic diarrhea, Johne's disease is a possibility (11). Johne's disease is characterized by dilated lymphatics and dilated villi, often obliterated by chronic inflammatory

cells, specifically epitheloid cells and giant cells containing acid-fast mycobacterial organisms (16,17). Bovine virus diarrhea and salmonella produce a marked inflammatory reaction in the mucosal surface of the villi, resulting in an alteration of normal architecture of the villi with inflammatory cell invasion of the lamina propria (9,17). Certainly, either one of these diseases would interfere with normal physiologic absorptive processes and cause an increased passive secretion of fluid into the lumen of the bowel, thus producing diarrhea.

B. *Decreased intestinal absorption* to unmask a high secretory rate is a second possible cause. This has been postulated to exist in man and animals; although possible, it is not a probable cause of secretory diarrhea (3).

C. *Mucosal cell secretion* is the third cause of secretory diarrhea and, in fact, has been studied extensively in relationship to human cholera (18,19). Specifically, investigators have found that the enterotoxin from the cholera organism will stimulate the enzyme adenyl cyclase. Adenyl cyclase converts adenosine triphosphate (ATP) to cyclic AMP. Cyclic AMP then stimulates the secretion of fluid and electrolytes from the mucosal cell into the lumen of the bowel, causing diarrhea (20,21,22,23). Other agents that can cause stimulation of adenyl cyclase and fluid secretion include prostaglandin F2α and theophyllin (24). Prostaglandins are released during the inflammatory response and thus whenever inflammatory conditions of the bowel occur, prostaglandins are likely to be released and may be part of the pathogenesis of diarrhea associated with these disease entities. Recently, prostaglandin inhibitors, specifically indomethacin, are being utilized to decrease prostaglandin release and thus possibly ammeliorate the diarrhea in some inflammatory bowel diseases. Clostridium perfringens toxin has also been proven to stimulate adenyl cyclase (25,26).

3. *Inhibited absorption* is the third cause of diarrhea. This possibility exists but is rare even in man. Here it is usually a congenital disease and has not been recognized in animals to date. When it occurs in man, it is associated with a decreased activity or lack of a specific enzyme in the intestinal mucosa.

4. Altered mucosal permeability is the fourth factor involved in the pathogenesis of diarrhea. Mucosal permeability may be altered in two ways:

A. Change in the surface area such as may occur with sprue (27,28), corona virus in calves (29), malabsorption syndrome (28), and Johnes disease (17). Lymphosarcoma will also obviously cause a change in the surface area as the mucosa becomes infiltrated with neoplastic cells (14).

B. The second possibility is an abnormality of the mucosa, resulting in a change in surface area. This is also possible, but is not likely and has not been shown to exist in large animals to date.

5. Deranged motility is the fifth factor in the pathogenesis of diarrhea. The lack of motility will cause stasis and bacterial overgrowth with possible peritonitis. Increased motility has been thought to be a part of the pathogenesis of diarrhea seen in man with "irritable bowel syndrome," "diabetic diarrhea," diarrhea associated with post-vagotomy or total gastrectomy. Although the exact pathogenesis of diarrhea associated with either of these entities is not known, increased motility has been implicated.

At this point I want to emphasize that when clinicians auscult the abdomen of a cow or a horse, borborygmus may be heard which is an admixture of fluid and gas in the intestinal tract and cannot be equated with intestinal motility. Many students believe that borborygmal sounds are the same as intestinal motility. Nothing could be further from the truth. In fact, it has been shown many times that increased borborygmal sounds occur with increased fluid in an atonic intestinal tract. Certainly intestinal peristalsis cannot be equated with clinically detectable borborygmal sounds. This fact must be emphasized as we relate it to the therapy of the animals with diarrhea.

Let us further evaluate intestinal motility. Basically, there are three types of intestinal motility: (a) segmentation of the bowel, (b) pendular movements of the bowel, and (c) peristaltic movements of the bowel (3).

5a. *Segmentation* occurs at irregular intervals with contraction of the circular muscles forming a sausage-like tube with contraction at specific points. These areas of contraction relax and then another area of contraction occurs between the previous two areas of contraction. This serves primarily as mixing and also an impedance to the flow of ingesta. The lack of segmentation type motility would result in rapid flow of ingesta along the digestive tract and be associated with diarrhea.

5b. *Pendular movements* of the bowel are basically swaying of the intestinal coils within the omental sling. This serves primarily for mixing and enhanced absorption of nutrients across the intestinal lumen.

5c. *Peristalsis,* perhaps the most important and certainly the most commonly considered aspect of motility of the bowel, serves to propel ingesta along the intestinal tract. Also important is reverse peristalsis which occurs commonly in the colon, especially from the mid-part of the colon orally toward the cecum. Reverse peristaltic movements impede the flow of ingesta and some oral flow of ingesta has been shown to occur in the horse (30), cat (31,32) and man (33). In fact, increased peristaltic movements in the colon have been associated with constipation, whereas diarrheic situations may be associated with decreased peristalsis (34). This seeming paradox is exactly the opposite of what was taught to students, both veterinary and medical, several years ago.

Now then, if diarrhea is *not* associated with an increased peristalsis, what is it associated with? Specifically, diarrhea is associated with a decreased transit time. Transit time is the time for ingesta to flow from the stomach to the rectum. In diarrhea the transit time is decreased or shortened, whereas in animals with constipation or obstruction of the bowel, transit time is prolonged and certainly this has been well documented in calves, most recently by Dr. David Ward at Cornell University (35).

Diarrhea is typically associated with certain electrolyte losses and leads to severe dehydration with which we are all familiar. This can be best illustrated in the young neonatal calf with profuse diarrhea which becomes dehydrated. Whether the disease is colibacillosis, salmonellosis, or enterotoxemia or viral enteritis (associated with reovirus, rota virus or the corona virus), it results in similar acid-base and electrolyte changes. These would include: (a) *acidosis* with a low bicarbonate, (b) *potassium* would be elevated to the point where the calf may die of hyperkalemia, and (c) the *sodium* may be variable, usually nearly normal, and the same exists with chloride (36,37,38,39). The glucose in these calves is usually low, sometimes resulting in the signs of hypoglycemic encephalopathy (40). Thus, when treating a calf with sunken eyes, loss of skin turgor, dry nose, and other clinical signs of severe dehydration and water loss, we could anticipate that the animal needs to receive bicarbonate-rich balanced fluid containing dextrose (36,37).

If we quantitate our clinical signs from a 0 to 4+, a slight diarrhea with slight dehydration indicates a mild change in the bicarbonate from the normal of 25 to 20 and a severe acute profuse diarrhea and dehydration is often associated with a 4+ (most severe) acidosis (Table 1).

Based on this type clinical assessment, a calf that weighs 110 pounds or 50 kilograms, with an assumed extracellular fluid volume of approximately 50% in the neonatal animal, has approximately 25 liters of extracellular fluid. The calf is 4+ dehydrated. This is a 20 mEq./L. deficit (obtained from Table 1) which needs to be replaced. The total deficit is 25 liters x 20 mEq./L. or 500 mEq. of bicarbonate. One gram of sodium bicarbonate contains 12 mEq. of HCO_3; thus, 500 divided by 12 gives 42 grams of sodium bicarbonate that is needed to correct the body deficit of bicarbonate created by the acidosis. How do we give this sodium bicarbonate? It could be given 5 grams/liter in lactated Ringer's, giving a mild hypertonic solution, or could be given as 13 grams/liter as an isotonic sodium bicarbonate solution or it could be given as 50 grams of sodium bicarbonate (a 5% solution) to correct the acidosis immediately followed with an isotonic solution for volume replacement. There is not a single best way to give this amount of bicarbonate. As long as we know the rationale and the limitations of each method we utilize, we will be providing effective rationale therapy to the sick calf. In essence then, when treating a calf with severe diarrhea and acidosis, we need an isotonic or slightly hypertonic solution coupled with glucose to prevent hypoglycemia, bicarbonate to correct the acidosis, and a balanced electrolyte, as possible. The single most important fact in correcting the acidosis is volume replacement, then bicarbonate.

Diarrhea is often associated with a severe acidosis whether the diarrhea is due to salmonella, winter dysentery, bovine virus diarrhea, parasites, chemicals or plant poisoning. However, the diarrhea must be acute and profuse if acidosis is to be expected. If the diarrhea is chronic and not profuse, the animal is likely to be compensated metabolically and although dehydrated severely may not be acidotic since the diarrhea was not acute and profuse.

The fluid therapy of large animals with diarrhea closely approximates that of calves except for the volume of replacement that is needed. It should be emphasized that volume replacement is the single most important key to correction of fluid and acid-base disturbances in adult cattle. A guide for fluid volume replacement that can be used clinically is presented in Table 2.

Obstruction or lack of feces is the next major topic to consider under problems of the lower gastrointestinal tract. Obstructive disease in the cow is

Table 1. Clinical Guide for Predicting the Acid-Base Status of a Bovine Patient
(The guide is based on the slightest detectable change in hydration, 1+, and the more severe, 4+.)

Clinical Signs*	Hydration**	Base Excess mEq/L*	Estimated Bicarbonate mEq/L
Fluid distended rumen - very scant feces	4+ dehydration	+20 B.E.	50
Splashy rumen - scant feces	3+ dehydration	+15 B.E.	45
Moderate distention - scant feces	2+ dehydration	+10 B.E.	40
Doughy rumen - firm feces	1+ dehydration	+5 B.E.	35
NORMAL	NORMAL	0 B.E.	25 ± 5
Slight diarrhea	1+ dehydration	-5 B.E.	20
Mild diarrhea	2+ dehydration	-10 B.E.	15
Moderate diarrhea - acute	3+ dehydration	-15 B.E.	10
Severe diarrhea - profuse, acute	4+ dehydration	-20 B.E.	5

*The correlating clinical sign for the prediction of alkalosis is abdominal distention and for acidosis it is the appearance of a tucked up (gaunt) cow.
**The hydration status is based on the combination of lack of skin turgor in the mid-neck area and the retraction of the eye in the socket.

Table 2. Guide to Fluid Volume Replacement for a 500 kg. (1,100 lb.) Cow

Severity of Dehydration	Eyes	Loss of Skin Turgor	Fluid Loss as % of Body Weight	Fluid Replacement Needed
+1	lack normal brightness	barely detectable	5 x 500 =	25 liters
+2	slightly sunken	obvious slowness	7 x 500 =	35 liters
+3	moderately sunken	slow to retract	9 x 500 =	45 liters
+4	marked sunken	remains raised	12 x 500 =	60 liters

usually associated with typical acid-base and electrolyte aberrations (41). This includes obstructive diseases from the omasum to the colon and would include: left abomasal displacement, right abomasal displacement, abomasal volvulus, intussusception, cecal dislocation, cecal volvulus, vagal indigestion (subgroups abomasal impaction, pyloric stenosis), and possibly small intestinal volvulus. In a series of obstructive diseases in cattle, we evaluated the electrolyte and acid-base statuses which are presented in Table 3. In each disease there is a tendency for a normal sodium, and hypokalemia is a prominent finding. The low potassium may be associated with decreased intake of roughage which is high in potassium, and continued renal potassium excretion. The renal potassium excretion continues despite the lack of intake and in fact may deplete the body of potassium. Another factor is the cellular shift of hydrogen and potassium. During alkalosis potassium goes into the cell and hydrogen comes out to neutralize the bicarbonate, resulting in the hypokalemia in the plasma. If this condition continues long enough, the cells become depleted because of continued renal loss of potassium. The chloride is perhaps the most significant change associated with obstructive disease of the bovine. It is almost always low and occurs because of continued abomasal secretion despite the fact the animals are ill and often anorectic. The abomasal juice, rich in chloride, is secreted into the lumen of the abomasum. The secretion is retained in the abomasum or is refluxed or vomited through the omasal canal back into the rumen, giving a large trap of excess choride retained in the rumen. This chloride trap results in a net increase in bicarbonate in the plasma which is generated in the kidney to give us anion balance (42). It should be remembered that the abomasum secretes between 30 and 35 liters in a 24-hour period of a very low pH material (43). This is a tremendous amount of chloride ion that is secreted each day. The bicarbonate increase results in a metabolic alkalosis. When we relate the chloride to the bicarbonate, there is an inverse relationship (r = 0.75). The lower the chloride, the higher the bicarbonate. This would be expected from the relationship already discussed.

Clinically, the impression of abomasal reflux can be detected by examination of the cow by percussion and a ballottement of the rumen. The normal rumen occupies approximately the left half of the abdomen of a cow, whereas with abomasal reflux, the rumen continues to enlarge, taking on an almost L-shaped appearance in the ventral abdomen where the ventral sac enlarges toward the right side. As one would expect, the rumen consistency becomes more fluid as more abomasal secretion is refluxed into the rumen. This can be detected by ballottement of the rumen and rating the consistency of the rumen from 0 to 4+ (see Table 1). Also, the normal cow that is anorectic and off feed is likely to be gaunt and tucked up, whereas the cow with obstructive disease is more rotund and has some fullness of the abdomen, especially when viewed from behind. This appearance of fullness we would not expect from a cow that is off feed and anorectic. Quantitative estimation of the severity of our clinical findings on a scale from 0 to 4+ will be an aid in therapy. A cow with obstructive GI disease between the omasum and the cecum would be expected to have a hypokalemic hypochloremic metabolic alkalosis, the severity of which varies with the choride trap. The clinical signs of alkalosis are most often sunken eyes, lack of skin turgor, and change in rumen consistency. Ballottement of the rumen and the use of Table 3 will provide guidelines as to the severity of the alkalosis associated with GI stasis and, in fact, can offer a reasonable prediction of the bicarbonate value. Thus, with a 4+ dehydration and obstruction, we would expect a base (B.E.) excess of approximately 25 mEq./L. (Table 1).

What types of fluids could be used to treat this type of alkalosis? We could use lactated Ringer's, a safe solution; sodium chloride, which is a mild acidifying solution; we could use approximately equal strength

Table 3. Acid-Base and Electrolyte Values in Cattle with Obstructive Gastrointestinal Disease

Disease	No. of Cases	Sodium*	Potassium*	Chloride*	Bicarbonate*
Left Abomasal Displacement	75	137 ± 0.6	3.5 ± 0.1	86 ± 4.0	27 ± 0.7
Right Abomasal Displacement	18	133 ± 1.0	2.9 ± 0.2	81 ± 3.0	34 ± 2.5
Abomasal Impaction	12	136 ± 1.2	3.3 ± 0.2	86 ± 3.7	38 ± 3.0
Intussusception	5	134 ± 2.4	3.3 ± 0.4	86 ± 4.4	35 ± 4.4
Cecal Volvulus	4	134 ± 2.1	3.1 ± 0.2	91 ± 3.0	32 ± 2.4
Normal Values	-	139 ± 2	4.0 ± 0.5	103 ± 4.0	25 ± 5.0

*Values - expressed as mEq/liter.

sodium chloride (5 gm/L) and potassium chloride (4 gr/L); potassium chloride and ammonium chloride, or hydrochloric acid, which is too drastic to be given intravenously (Table 4).

Table 4. Electrolyte Composition of Common Fluids in Large Animal Practice and Compared to Patients with Acid-Base and Electrolyte Disorders

Fluid	NA*	K*	CL*	HCO_3*
1. Patient with alkalosis (2+)	140	3.0	80	40
2. Normal bovine plasma	140	4.0	105	25
3. Lactated Ringer's solution	130	4.0	111	27 (lactate)
4. Isotonic sodium chloride	154	--	154	--
5. (4 gms. potassium chloride/L; 5 gms. sodium chloride/L)	85	56	141	--
6. (4 gms. ammonium chloride/L; 5 grs. potassium chloride/L)	75	75	150	-(75)
7. Isotonic hydrochloric acid	--	--	150	-(150)
8. Patient with acidosis (severe)	140	6.0	100	5
9. 1.3% (isotonic) sodium bicarbonate	156	--	--	156
10. 5% sodium bicarbonate (50 gms/L)	600	--	--	600
11. Lactated Ringer's & 5 gm $NaHCO_3$/L	190	4.0	111	60 + (27) lactate
12. 6% dextrose	--	--	--	--

*Expressed as mEq/L

To calculate how much acidifying fluid to give alkalotic cows, in a 500-kilogram cow, assume 30% of her body weight is extracellular fluid, which gives 150 liters of extracellular fluid with a base excess of moderate severity (2+). The base excess is +10 mEg/L (Table 2). This is 1,500 mEq. of base that needs to be titrated using an acidifying solution. This could be accomplished with 20 liters of the following solution containing 108 grams of potassium chloride, 80 grams of ammonium chloride, and given at the rate of five liters per hour (the safe rate in the adult cow). If, however, one is not sure of the specific acid base and electrolyte changes associated with any disease, be it obstructive or diarrheic, one should consider giving the safest solution possible which is a balanced isotonic polyionic solution and remember, the *"dumbest kidney is smarter than the most intelligent clinician!"*

The next most common disease in the lower G.I. tract is blood in the feces. Blood in the manure can be divided by its appearance as bright red blood coming from the lower intestinal tract, i.e., the rectum or colon, or dark black blood coming from higher in the intestinal tract. Bright red blood in the feces is commonly associated with coccidiosis, winter dysentery, occasional cases of salmonellosis, repeated rectals, sadism, or other entities and most recently we have had a case of renal disease associated with bright red blood in the stool.

Black feces are commonly associated with abomasal ulcers and certainly this comes to mind to most clinicians when they see dark black feces (43). However, other causes of dark black feces would include duodenal ulcers, upper G.I. parasitism, or hemoptysis. Hemoptysis is often forgotten as a cause of blood in the stool as these cows cough up blood from the lungs and swallow it, which may result in a dark black stool. There are other causes of dark black stool and bleeding in the G.I. tract as well. Blood in the stool can be confirmed by the use of the occult blood test (Guiac test).

Abomasal ulcers do not always result in the dark tarry stools as there are at least four types or classifications of abomasal ulcers. This would include: (a) abomasal ulcers associated with slight erosion and ulceration, (b) abomasal ulcers associated with hemorrhage and typical dark tarry stool, (c) the ulcers associated with perforation and acute circumscribed peritonitis, and (d) the ulcers that perforate and cause acute diffuse peritonitis. Most clinical experience would emphasize that ulcers that perforate do not bleed very much and the ones that bleed will often not perforate. This should be important in the medical therapy of these diseases.

Abomasal ulcers of the first type, the ones with slight erosion and mild ulcers, are often secondary to another disease such as septic mastitis, septic metritis, or peritonitis. The feces are often fetid, dark, and loose. There is a minimal anemia associated with this type of ulceration as the blood loss is only slight and, as this primary disease heals, so do the ulcers. However, the ulcers typically associated with dark tarry feces are often stress-associated and occur early in lactation and can produce a severe anemia to the point where the animal may die (43). They are often single bleeding ulcers and, in fact, the cow may bleed out into the lumen of the abomasum from blood loss. Another point to be emphasized is that dark tarry feces may be a sign of lymphosarcoma as lymphosarcoma has a predilection for the abomasum and may present as a bleeding ulcer and, thus, dark tarry stools should remind the clinician that lymphosarcoma should be considered suspect (14).

In conclusion, one should remember that there are two major types of problems associated with lower G.I. tract: (1) diarrhea, and (2) obstruction, each associated with its own characteristic acid-base and electrolyte disturbances. Acidosis with diarrhea and alkalosis with obstruction. If the clinical acid-base and electrolytes signs are not obvious, treatment with a balanced polyionic solution is appropriate.

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