



Optimizing the Intestinal Health Of Baby Calves

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The intestinal mucosa is a single cell layer that separates the intestinal contents from the biological compartments of the animal. This expansive surface facilitates nutrient absorption while protecting the body from both the normal beneficial flora resident within the intestinal lumen as well as unwelcome pathogens. The intestinal mucosa provides not only a physical barrier to intrusion, it is also armed with more active methods of keeping intestinal microflora in check.

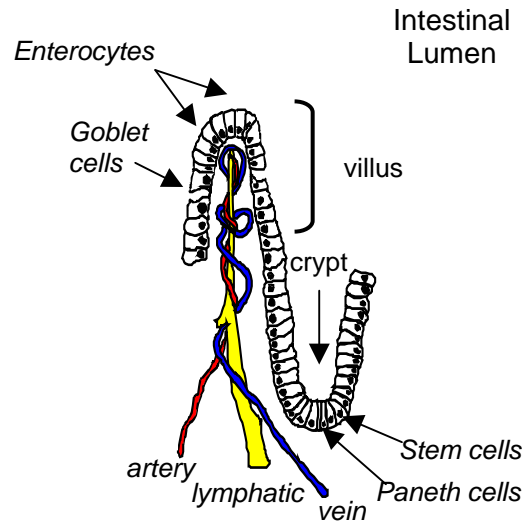
The first 3-4 weeks after birth may well be the most challenging period of the calf's life. It is certainly a period of great change. The calf is born with a sterile digestive tract that rapidly becomes populated with organisms. The calf is also dependant on appropriate management and administration of colostrum for passive transfer of immunity, while at the same time beginning a transition process from monogastric to ruminant digestion. A sizable list of challenges can readily be assembled.

The more we learn and understand about the function and environment of the small intestine, the more effective our efforts to manage the calf and it's environment for optimum growth and performance. This review provides a brief discussion of the structure and function of the small intestine, an overview of innate intestinal defense mechanisms, the effects of scours on intestinal health and a summary of management practices, feed additives and supplements that benefit intestinal health.

Structure Of the Intestinal Mucosa

The mucosa, or lining of the small intestine is made up of villi and crypts. Figure 1. Villi project into the open space, or lumen, of the small intestine and are mainly involved in nutrient absorption.

Figure 1.



adapted from Austgen et al

Each villus is well supplied with blood and lymph vessels that rapidly move absorbed nutrients away from the digestive tract and into the body. Crypt cells, on the other hand, are primarily concerned with secretion of substances, including water, into the intestinal lumen.

Enterocytes are the absorptive cells of the villi. Goblet cells produce mucin that primarily serves a protective function. Although not shown in Figure 1, another type of cell found on the villi is the enteroendocrine cell. These cells are part of the endocrine system and continuously test and evaluate the intestinal contents. When stimulated, they secrete hormones into the bloodstream that communicate messages to other structures and organs to modify their activity in response to conditions within the intestine. The fourth type of mucosa cell is located in the crypt. They are called Paneth cells, and produce antimicrobial substances. The cells that make up the intestinal mucosa are short-lived. The life span of villus cells is 4-6 days

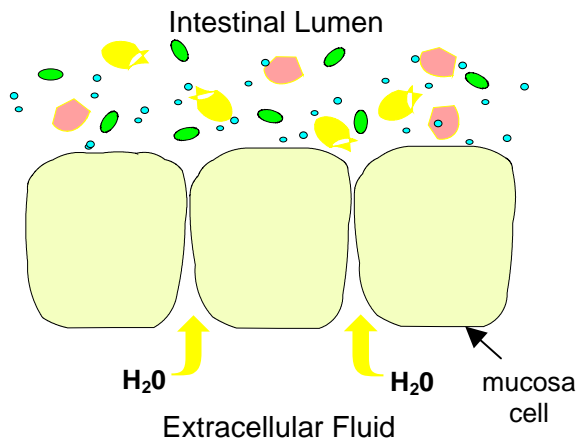
while Paneth cells are active for about 14 days. Stem cells located near the base of the crypt are the source of enterocytes, goblet cells, enteroendocrine and Paneth cells. Stem cells develop and differentiate as they migrate from the crypt up to the villus.

Water Movement In the Small Intestine

In healthy animals, large amounts of water are regularly secreted into the small intestine to help digest and absorb nutrients. Most of this water is recovered as the nutrients are digested and absorbed. As food enters the small intestine, water readily “leaks” between the mucosa cells of the upper small intestine into the lumen. During digestion large food particles are broken down to small absorbable nutrients, increasing the concentration of particles inside the intestine. This concentration, referred to as osmotic pressure, is much greater inside the intestine than it is in the cells and fluids of the body surrounding the digestive tract. Since water flows toward areas of high osmotic pressure, water moves from the body into the intestinal lumen. Figure 2.

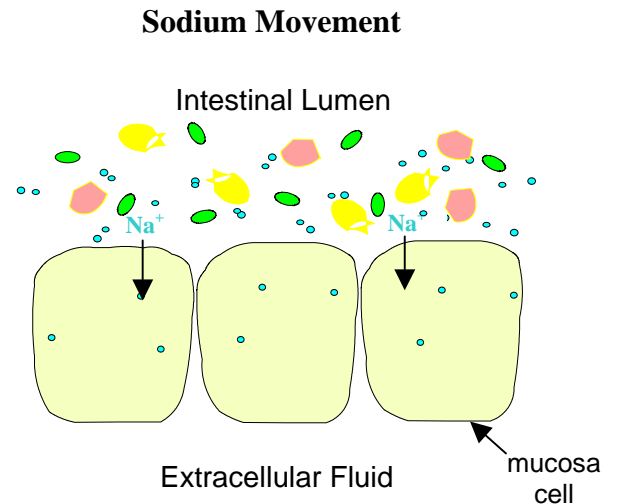
Figure 2.

Water Movement Into the Small Intestine



Water is resorbed from the digestive tract as a result of nutrient absorption, with sodium (Na^+) playing an important role in this process. As a rule: *water follows sodium*. Sodium is free to move across mucosa cell membranes in response to osmotic differences, moving from areas of higher osmotic pressure to areas of lower osmotic pressure. Figure 3.

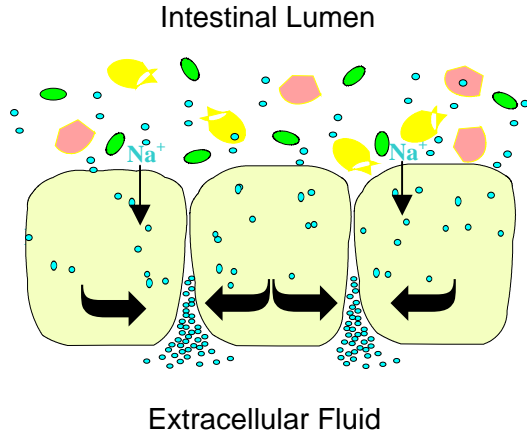
Figure 3.



Although this passive diffusion of Na^+ results in water movement out of the digestive tract, it is insufficient for adequate water resorption. Sodium is also actively moved across the mucosa cell membrane along with other nutrients.

For example, amino acids and carbohydrates are co-transported with Na^+ out of the lumen and into the mucosa cells of the small intestine. Once inside the cell, Na^+ is rapidly pumped into the extracellular fluid surrounding the cell, away from the intestinal lumen. As a result of these nutrient movements, a series of osmotic gradients are created which move water from the lumen into the cell, and then from the cell into the extracellular fluid. Figure 4. The Na^+ and water then diffuse into the blood stream.

Figure 4.



This ability to concentrate Na⁺ in the extracellular fluid surrounding mucosa cells, drawing water from the digestive tract, increases as food particles move through the small intestine. By the time food reaches the large intestine, about 80% of the water has been resorbed.

Innate Defenses of the Intestinal Mucosa

Within the digestive tract, examples of innate defenses include physical processes such as peristaltic movements of the intestine, shedding of epithelial cells, chemical barriers such as gastric acidity, bile acids, antimicrobial peptides and mucus as well as water secretion. The last three – water, mucus and peptide secretion -- will be reviewed in this text.

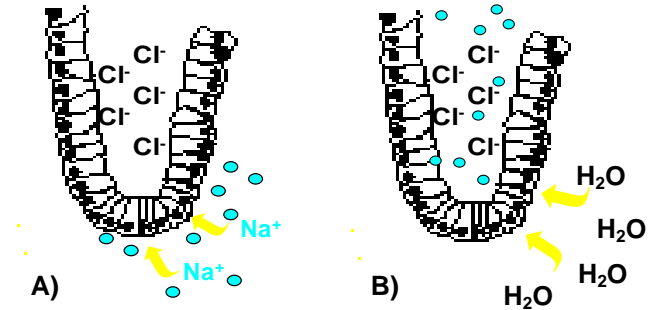
Water Secretion. A simple method of responding to the presence of intestinal pathogens is water secretion. The idea is that rapid and increased flow of fluid across the intestinal epithelium flushes organisms from the intestinal lumen preventing attachment and maybe dislodging some that are already adhered. The presence of bacterial factors, such as cholera and *E. coli* toxins, initiates intestinal secretion of electrolytes and water.

This process involves moving water into the intestine through specific action of crypt cells. By pumping chloride ions (Cl⁻) into the crypt space in response to bacterial toxins, crypt cells actively

draw water into the intestine. These Cl⁻ ions attract sodium ions (Na⁺) into the crypt space, increasing the local osmotic pressure. Figure 5A. As the osmotic pressure increases, water is pulled into the intestine. Figure 5B. Some bacteria, such as cholera, cause this pump system to lock in the “ON” position. In addition, invasive organisms such as *Salmonella typhimurium* and certain strains of *E. coli* infect the epithelial cells causing the host to initiate this form of secretory diarrhea.

Figure 5.

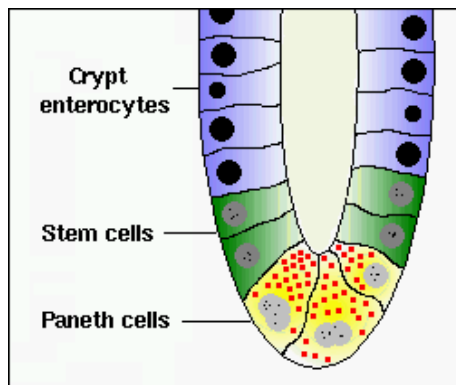
Water Secretion Into the Crypt Space



Mucus secretion. Goblet cells located on the surface of the intestinal villi produce highly complex mucus glycoproteins, or mucin, which coats the upper surfaces of the villi. This gel-like layer provides a front line defense against pathogens. The carbohydrates in the mucus layer are quite diverse and provide numerous binding sites for both commensal and pathogenic organisms. In this way, the mucus layer serves as a platform for microbial colonization. This process may slow microbial interaction with epithelial cells of the villi and help prevent injury. In addition, the mucus layer may also enhance removal of microorganisms through peristaltic movements. Mucus volume and composition, intestinal motility and fluid flow rate influence whether a harmful or beneficial effect occurs as an outcome of microbial attachment. Probiotic organisms such as lactic acid bacteria have been shown to stimulate mucus production in the small intestine (4), enhancing the beneficial effect of the mucus layer.

Antimicrobial peptides. Stem cells located near the base of the intestinal crypts continuously produce cells that differentiate and repopulate the intestinal mucosa. The turnover rate of the intestinal mucosa is rapid with total repopulation occurring every four to six days. Closely associated with stem cells are the Paneth cells, (Figure 6), which are strategically located at the very base of the crypts. Paneth cells help protect the cell renewal process from bacterial infestation by providing a chemical barrier of immunity.

Figure 6.



Colorado State University

Paneth cells actively sense bacteria and release antimicrobial peptides, called defensins. Defensin production is an innate immune response that kills bacteria immediately on contact without having to produce specific antibodies. These defensins interact with the bacteria, causing pores to form in the bacterial membrane that lead to cell death. By inhibiting bacterial colonization of the crypt, Paneth cells protect stem cells and allow their replication to proceed continuously to maintain mucosal integrity.

Defensins appear to be an important aspect of immunity even in very young calves. One-day-old calves were dosed with a non-fatal dose of *Cryptosporidium parvum*, which typically causes diarrhea for 5-10 days (10). This organism invades the intestinal epithelium causing blunting of the villi, tissue inflammation and increased crypt cell

growth. Calves were euthanized at 5 days of age when the first signs of scours appeared. The intestinal tissues of the calves showed up to a 10-fold increase in defensin mRNA, indicating increased defensin production in response to cryptosporidium infection.

Paneth cells also appear to communicate with the body. For example, Paneth cells have been shown to respond to the presence of bacteria by promoting development of blood vessels in the intestinal lining (7), and certain defensins have been shown to enhance systemic IgG (6).

Water Loss (Diarrhea)

Scours is the most prevalent disease of pre-weaned calves in the U.S., accounting for 62% of pre-weaned heifer calf deaths on dairy farms. Conditions that cause water loss can have a significant impact on intestinal health. The converse is also true. Pathogens, feed characteristics and management influence digestive function and can result in water loss through the digestive tract. There are four types of digestive water loss. A diarrheic animal may actually suffer from more than one type of water loss at the same time.

Increased Permeability. Microbes cause inflammation and damage to the intestinal mucosa resulting in increased water movement into the intestine. This type of water loss is commonly caused by viruses (rotavirus, coronavirus) and protozoa (coccidia, cryptosporidia). Inflammation may also lead to host-generated hypersecretion.

Hypersecretion. This type of water loss is similar to increased permeability in that large amounts of water move into the intestine, but there is no tissue damage. Bacterial enterotoxins stimulate cellular pumps in the crypt cells of the intestinal mucosa to secrete large amounts of ions into the intestinal lumen. These ions draw water into the small intestine. Hypersecretion in calves is commonly caused by *E. coli*.

Malabsorption. Epithelial damage of the small intestine reduces nutrient absorption. Viruses and

protozoa damage the villi in the small intestine leading to villous atrophy, and can damage the mucosa of the large intestine as well. Normal amounts of water may be secreted into the digestive tract, but tissue damage results in poor nutrient and water absorption. Malabsorption results in increased nutrients reaching the large intestine. These additional nutrients can cause bacterial overgrowth and excessive production of volatile fatty acids (VFAs). As a result, osmotic changes can occur that increase fluid loss.

Maldigestion. Changes in feed management may lead to maldigestion. A sudden change in feed, use of poor quality ingredients, the presence of feed allergens or other detrimental factors and digestive disorders can lead to maldigestion. Maldigestion usually results in malabsorption.

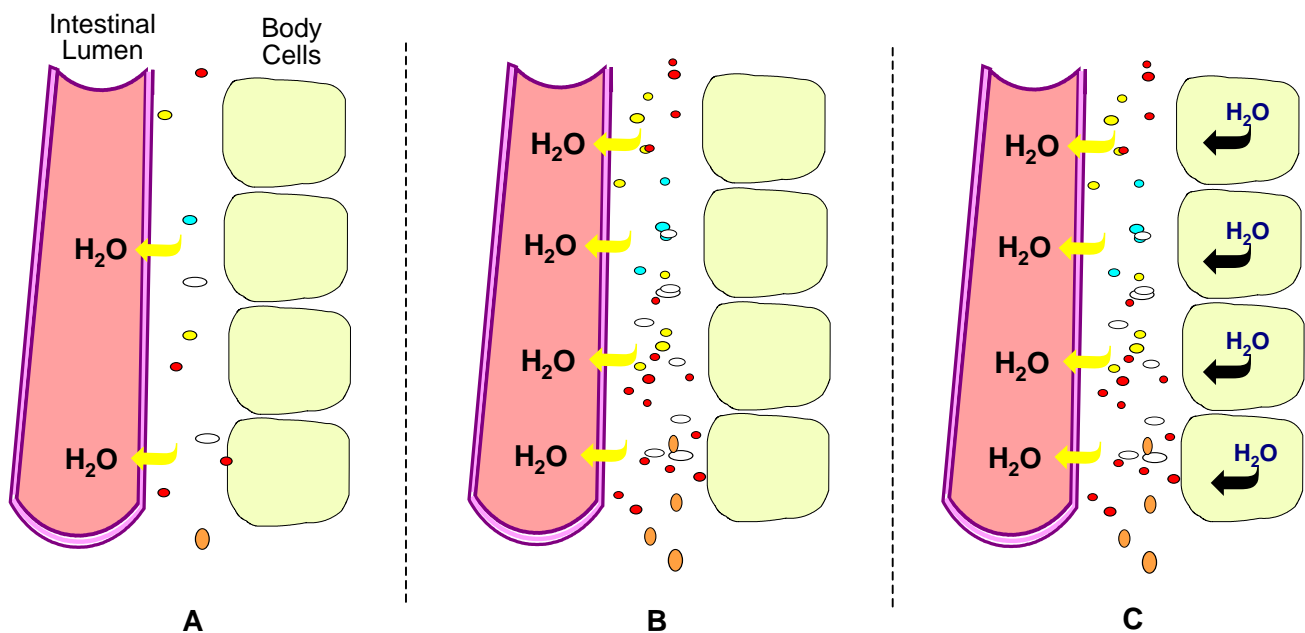
Dehydration. A calf can lose as much as 6% of its body weight before showing visible signs of dehydration. Giving fluids too little, too late allows progressive fluid loss. As a result, the calf's condition continues to deteriorate. Most calves that die of scours usually die from loss of water and electrolytes rather than any direct action of pathogenic organisms.

During dehydration water moves from the extracellular fluid into the digestive tract. Water moves from the blood and the space between cells (the interstitial space) into the intestinal lumen. Figure 7A. As more water moves into the intestine, the concentration of substances in the extracellular fluid rises, Figure 7B, increasing its osmotic pressure. Since water moves toward areas of higher osmotic pressure, water leaves the cells and moves into the extracellular fluid. Figure 7C. This process of cellular dehydration helps maintain the plasma blood volume. (A more detailed description of dehydration can be found in [Electrolyte And Water Balance In Baby Calves.](#))

Efficacy of Treatment. The amount and timing of electrolyte replacement therapy is critical for rapid recovery from dehydration and to minimize the impact on the intestinal mucosa. The focus of any treatment plan should be on replacing lost fluids and restoring acid base balance. Enterotoxigenic *E. coli* causes a hypersecretion type of water loss. In this situation, only about 60% of the electrolyte solution is absorbed (12), so the frequency of administration needs to be increased. In this case, 40% of the electrolyte solution will pass through the calf's digestive tract, adding to the calf's fecal

Figure 7

Process of Dehydration Due to Scours



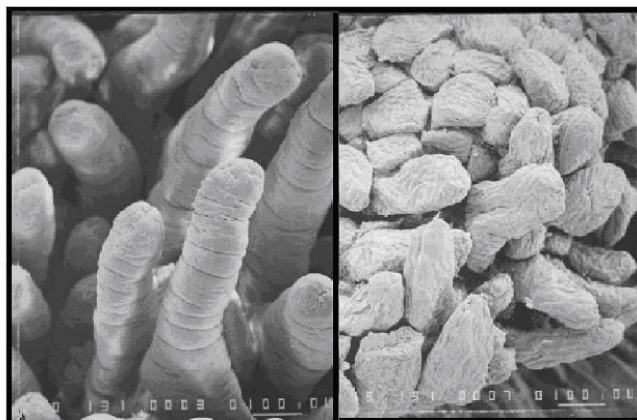
water loss. This makes the diarrhea appear to be worsening with electrolyte therapy even though the treatment is effective.

Rotavirus, coronavirus and cryptosporidia invade and damage the intestinal villi causing an increased permeability type of water loss. These organisms tend to affect calves over a week old causing a somewhat slower rate of water loss and a more prolonged infection than with Enterotoxigenic *E. coli*. Electrolyte therapy reduces the metabolic acidosis associated with these infections. As a result, the suckling reflex increases, helping the animal to recover without other treatments.

Milk/Milk Replacer Feeding. Substituting an electrolyte solution for milk replacer does nothing to correct fluid loss. When normal digestive and absorptive functions of the intestine are impaired, calves cannot absorb adequate nutrients from the diet. Since young calves have precious little in the form of stored nutrients to sustain them, digestive and absorptive problems can progressively lead to rapid weight loss, weakness and death. This situation is made worse when milk replacer is withheld during the treatment process.

Withholding milk replacer does reduce nutrients available for gut pathogens, but also reduces nutrients for the calf. This reduction in nutrients not only compromises the normal gut flora, it also reduces nutrients available for immune function and contributes to intestinal villi atrophy. The villi on the left of Figure 8 are healthy intestinal villi of a pig at weaning.

Figure 8.



University of Missouri

The picture on the right shows villi two days later before the pig has adjusted to the new diet, and clearly shows the effects on the intestinal mucosa of withholding nutrients.

The digestive tract requires more energy to keep it going than any other organ in the body. If the inflow of nutrients is greatly reduced, the digestive tract begins to shut down, conserving energy by reducing functions. Villus atrophy reduces nutrient absorption and compromises the protective barrier function they provide against pathogens. There is strong evidence that withholding nutrients also prolongs the duration of diarrhea and slows recovery.

Management Factors Affecting Intestinal Health

Whether intentionally or accidentally, a host of management factors are brought to bear on the intestinal health of baby calves. We can reach all the way back to the last trimester of the dam for factors that affect the calf's susceptibility to disease and other stressors. Calving facilities, vaccinations, feeding protocol and sanitation procedures all deserve exploration, but are beyond the scope of this review. There are, however, three areas of calf management that have a direct and significant effect on the intestinal integrity of young calves and deserve some discussion.

Colostrum. Much has been written about the critical importance of the quality, quantity and timing of feeding colostrum. Colostrum management is arguably the single most important calf management factor that sets the tone for what will follow in the calf's life.

Colostrum is a critical source of immunoglobulins (Ig) or antibodies for the calf's immune system. IgA makes up 10-15% of the immunoglobulins in colostrum and protects mucus membranes such as those around the eyes, nasal passages and the intestines. Another 10-15% of colostrum immunoglobulins are IgM. This large antibody circulates in the bloodstream, protecting the calf from septicemia. If the integrity of the intestinal

mucosa were compromised to the extent that bacterial pathogens entered the calf's bloodstream, IgM would be a major line of defense. IgG comprises between 70-80% of immunoglobulins in colostrum. IgG is also the most plentiful immunoglobulin in the bloodstream. Its small size allows it to move out of the blood into other areas of the body, including the digestive tract. The amount of IgG secreted back into the small intestine over time is related to the amount circulating in the blood. The higher the IgG absorbed from colostrum, the higher the level in calf's bloodstream. The higher the IgG in the blood, the higher the percentage secreted into the small intestine. In the digestive tract, IgG can have a direct effect on pathogens and may also have a direct beneficial effect on the intestinal mucosa.

Nutrition. Calf nutrition is a broad subject area with many direct and indirect consequences on intestinal health. The calf's overall plane of nutrition is a broad category that has significant effects on its ability to maintain intestinal integrity. Stress conditions, at the most basic physiological level, decrease blood flow to the intestines, compromising the integrity of the mucosal barrier.

Milk replacer. Economic considerations and the desire to convert calves to ruminants as soon as possible after birth are major motivators behind the traditional approach of feeding a 20% protein, 20% fat milk replacer at a rate of one pound of powder per day. This formula and feeding rate provides enough protein and energy to support a calf up to about 115 lb. Any additional growth will come from the intake of starter feed. This situation can put a tremendous amount of stress on the calf, especially if there are any pathogen, weather or other stress factors that can quickly compromise intestinal health. Increasing nutrient intake through a higher feeding rate of milk replacer will go a long way toward providing the calf a better nutritional foundation. In this situation, the milk replacer formula should be appropriate for the feeding level for best growth and performance results. A variety of formula and feeding rate combinations are available. There are sizable differences in the economics of different programs.

Spending some time evaluating options can be well worth the effort.

Waste milk. One of the major advantages of milk replacer over waste milk is that it is a commodity with a known nutrient profile that can easily be adjusted to achieve specific results. Waste milk, on the other hand, can be quite variable over time, even from day to day. Although a gallon of waste milk will typically provide more nutrients than a gallon of a 20/20 milk replacer reconstituted to label specifications, the nutrient variability can cause digestive challenges and upsets. If waste milk variability is an issue, adjusting the solids content to a specific level by using appropriate amounts of a milk replacer, fortifier or extender can reduce nutrient fluctuations. Waste milk is also a potential source of bacteria and pathogens that can have a deleterious effect on intestinal health. Although pasteurization does not eliminate all bacteria from waste milk, it is an important safeguard with major impact on calf health.

Scours. Although the subject of calf scours was previously reviewed, management philosophies and approaches to scour treatments are quite variable and deserve an additional mention. While scours volume and consistency are important measures, they should not be the focus of attention. As previously mentioned, effective rehydration therapy often increases the amount of water passing through the calf. Basically, it is just simple mathematics. Water loss and intestinal damage due to the pathogen plus decreased ability to fully absorb the electrolyte solution equals increased water loss. This result runs counter to the desire to reduce output and solidify manure, and may lead to a reluctance to implement effective rehydration practices. Something is obviously out of perspective when 1 in 10 pre-weaned dairy heifers in the U. S. dies, most likely from scours. Implementing an effective rehydration program can certainly be a step toward reducing calf mortality.

From a practical standpoint, calf attitude will likely be a more realistic early measure of treatment progress. As rehydration is achieved and healing progresses, improvements in output volume and

consistency will follow. Creating an environment for healing should be the focus of a rehydration and scours treatment program.

Electrolyte solutions should be formulated to maximize water absorption and facilitate gut repair. A proper balance of sodium, glucose and amino acid(s) facilitate water absorption. Adequate levels of chloride and potassium help replenish the major electrolytes involved in water balance within the body. A brief review of several ingredients/supplements that facilitate gut repair and a return to normal function is provided in the next section. Several of these supplements can be incorporated into electrolyte products.

Ingredients/Supplements

Many ingredients and products are now available that demonstrate beneficial effects in the calf's digestive tract. The following list provides a brief description of several of the more common ingredients or supplements fed to calves to enhance or complement digestive and absorptive functions.

Direct-Fed Microbials (DFMs). DFMs are beneficial organisms that colonize in the digestive tract, produce organic acids and other beneficial compounds and compete against pathogens. A wide variety of organisms are used as DFMs. The primary DFMs used to colonize the small intestine are lactic acid bacteria (LAB). They are very rapid colonizers in the small intestine and compete very effectively against pathogens such as *E coli*. LAB have also been shown to enhance the production of protective mucin in the small intestine.

Fructooligosaccharides (FOS). FOS are naturally occurring plant sugars that provide a source of nutrients for beneficial bacteria in the large intestine such as Bifidobacteria. FOS have been

shown to increase volatile fatty acid (VFA) production in the large intestine and improve calcium and magnesium absorption. FOS cannot be digested by the animal or by pathogenic bacteria.

Mannan oligosaccharides (MOS). Mannan oligosaccharides contain yeast cell wall fragments. These fragments contain mannans, which competitively bind gram-negative bacteria, preventing their attachment to the intestinal mucosa. Since mannans are not digestible in the intestine, the bound pathogen likely passes through the digestive tract. MOS may also stimulate antibody production and enhance intestinal structure and function.

Plant extracts/spices. This group of feed ingredients includes allicin (garlic extract) and a variety of spices. These ingredients vary in their modes of action but proposed activities include stimulation of digestive enzymes, antimicrobial activity, immune stimulation, improved VFA production and feed intake enhancement.

Animal Plasma. Animal plasma is obtained by centrifuging whole blood into its major components, plasma and blood cells. The two main types of animal plasma are bovine (ruminant) and porcine (swine). These products provide a source of both protein and immunoglobulins, primarily IgG and are usually added to milk or milk replacer. In the digestive tract, IgG has a direct affect on pathogens and may also have a direct effect on the intestinal mucosa.

Glutamine/Glutamate are amino acids that have been shown to improve villi height and overall intestinal morphology during periods of stress and following injury. Both glutamine and glutamate provide a local fuel source for enterocytes, the absorptive cells of intestinal villi.

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