Diagnosis and Treatment of Infectious Enteritis in Neonatal and Juvenile Ruminants

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KEYWORDS

- Ruminant • Enteritis • Infection • Juvenile • Neonate • Diarrhea

KEY POINTS

- Common causes of infectious enteritis in neonate and juvenile ruminants include viral, bacterial, and protozoal pathogens.
- The most common presenting sign in ruminants with infectious enteritis is diarrhea.
- Diagnosis of the cause of enteritis has important zoonotic and herd health implications.
- Severity of clinical signs with similar pathogens may differ between calves and small ruminants.
- Treatment of enteritis involves supportive care to correct fluid and electrolyte imbalances, provision of nutritional support for the neonate, prevention and treatment of endotoxemia or sepsis, and pathogen-specific treatments when relevant and available.

PATHOPHYSIOLOGY

Several mechanisms of diarrhea are possible in ruminant neonates. This article summarizes the various mechanisms:

- Malabsorption
  - It is important to remember that, under physiologic conditions, more fluid is secreted into the intestinal lumen, and reabsorbed, compared with the ingested amount. Therefore, impaired reabsorption of fluids has a major impact on the fluid balance of the patient. Several diarrheal pathogens interfere with digestion and absorption by blunting intestinal villi, as observed with rotavirus and coronavirus infections.
- Osmotic
  - Increased solutes within the intestinal lumen osmotically pull more water into the lumen, thereby resulting in dehydration of the patient. Osmotic particles

include maldigested disaccharides, and increased D-lactate levels from bacteria fermentation of unabsorbed nutrients that enter the colon.

- Secretory
  - Specific pathogens, such as enterotoxigenic *Escherichia coli* (ETEC), stimulate cyclic AMP, thus increasing secretion of chloride (Cl), sodium (Na), and potassium (K) into the intestinal lumen, thereby drawing water into the intestinal lumen.
  - In addition, some pathogens denude the intestinal surface and cause villous blunting, resulting in maldigestion and malabsorption. This damage to the villous leads to proliferation of secretory crypt cells and increased secretory capacity of the intestinal wall.
- Abnormal intestinal motility
  - Decreasing intestinal transit time may lead to maldigestion and malabsorption because of inadequate time for digestion and absorption of the ingested feed material. This process further contributes to osmotic retention of fluid in the intestinal tract.
- Increased hydrostatic pressure
  - Disease conditions, including heart failure, renal disease, and liver disease, may result in increased hydrostatic pressure within the intestinal tract causing movement of water from extracellular tissues into the intestinal lumen, resulting in diarrhea.
- Gastrointestinal (GI) inflammation
  - Inflammation of the GI tract or the peritoneum (peritonitis) can exacerbate all of the above mechanisms of diarrhea. Increasing intestinal permeability or increasing hydrostatic pressure within the intestinal wall can increase fluid loss into the lumen. In addition, prostaglandin production stimulates fluid secretion into the lumen. Infiltration of the intestinal wall by inflammatory cells can also disrupt intestinal motility, increase intestinal secretion, and decrease absorptive function.

Diarrhea often results in fluid and electrolyte losses for the patient. As long as the ruminant neonate can compensate for losses, it will remain hemodynamically stable, and continue to nurse. However, if losses exceed intake, systemic effects will be observed on clinical examination. Fluid loss from the vascular compartment leads to hypovolemia (dehydration), hypotension, and shock. Metabolic acidosis develops as a result of intestinal and fecal loss of sodium bicarbonate, increased L-lactate from hypoperfused tissues, and increased absorption of L-lactate and D-lactate produced by bacterial fermentation in the intestinal tract.[1] As dehydration and acidosis worsen, clinical signs progress, leading to weakness, loss of suckle reflex, and recumbency. Vascular collapse and electrolyte imbalances can lead to heart failure, whereas death can also result from malnutrition and hypoglycemia in neonates. In addition, endotoxemia from gram-negative bacterial infection, such as *Salmonella* or *E coli*, can directly cause circulatory failure.

PATIENT HISTORY

Patient history should include information regarding the age and use of the animal (eg, dairy, beef, show animal), history of colostrum ingestion, duration and progression of diarrhea, age, and number of animals affected or dead in the herd. Assessment of housing, management, feeding, sanitation practices, and preventive health measures is also important. On-farm standard operating procedures regarding treatment protocols are important to obtain and review, especially when approaching outbreaks of

diarrhea. It is also important to ascertain whether there have been any recent dietary or husbandry changes (weaning), transportation, on-farm treatments, or addition of new animals.

PHYSICAL EXAMINATION

In clinic settings, ruminant patients should be examined in an area that can be isolated from other patients according to infectious disease control protocols. In farm settings, care should be taken to minimize cross-contamination between animals and particularly minimizing exposure to younger animals. In either scenario, the facility should be cleaned and disinfected following the examination. The examiner should wear personal protective equipment (eg, gloves, boots that can be disinfected, and coveralls) that are cleaned or discarded after handling the patient.

Although it is necessary to perform a complete physical examination in ruminant patients with enteritis, this article focuses on the techniques that are specific for organ examination in ruminants with enteritis. These techniques include the following:

- Assessment of hydration status: tacky or dry mucous membranes, decreased skin turgor, and eyeball recession (sunken eyes) indicate dehydration. Parameters for assessing dehydration in neonates are presented in **Table 1**.[2] Also, a previous issue (March 2009) covers this topic as well.[3] **Fig. 1** shows a calf with eyeball recession caused by dehydration.
- Signs of endotoxemia or septicemia: assess mucous membranes for color and capillary refill time. Assess the sclera for injected, dilated blood vessels. Septicemic calves may show evidence of hypopyon (**Fig. 2**) in the anterior chamber of the eyes, swollen joints, omphalophlebitis, or meningitis on physical examination. Evidence of sepsis negatively affects prognosis.
- Posture: the posture of the patient may indicate evidence of abdominal pain; for instance, abdominal distension, arching of the back (kyphosis), treading of the hind feet, and lying down with hind legs outstretched. In cases of overt abdominal pain, the possibility of surgical conditions should be investigated and ruled out. In primary cases of neonatal enteritis that do not show evidence of septicemia or endotoxemia, the attitude and posture of the animal can provide evidence of dehydration and metabolic acidosis. Recumbent animals with greater mentation deficits in general have more severe metabolic acidosis.

Table 1
Estimation of dehydration in calves with diarrhea by eyeball recession, skin tent, and increase in total protein

	Dehydration (% Body Weight)							
Factor	0	2	4	6	8	10	12	14
Eyeball Recession (mm)	0	1	2	3	4	6	7	8
Neck Skin Tent (s)	2	3	4	5	6	7	8	9
Increase in TP (g/dL)	0	0.2	0.5	0.7	1.0	1.2	1.4	1.7

Abbreviation: TP, total protein.
Adapted from Constable PD, Walker PG, Morin DE, et al. Clinical and laboratory assessment of hydration status of neonatal calves with diarrhea. J Am Vet Med Assoc 1998;212(7):991-6; with permission.

Fig. 1. Eyeball recession in a dehydrated calf. (*Courtesy of* Robert Callan, DVM, PhD, Colorado State University, Fort Collins, CO)

- Rectal temperature: body temperature may be either pyrexic, normal, or hypothermic in neonates with enteritis. Hypothermia generally indicates that the patient's body is decompensating. It may also be an indication of hypoglycemia. The presence of hypothermia is often a poor prognostic indicator.
- Body condition: poor body condition may indicate chronicity or malnutrition, which could be a compounding factor and worthy of further herd investigation with the client.
- Oral examination: examination for oral ulceration and hypersalivation (ptyalism) is important because some viral causes of enteritis can also cause oral lesions. The presence of a suckle reflex is important and helps to determine the most appropriate fluid therapy strategy. The presence of a suckle reflex makes oral nutritional support much easier and allows a more cost-effective treatment plan.
- Abdominal palpation, auscultation, percussion and succussion: abdominal palpation may help identify evidence of pain or allow palpation of abdominal viscera. Simultaneous auscultation and percussion (pinging) on the left and right abdominal walls aids in identification of viscera filled with fluid and air under

Fig. 2. Hypopyon in a calf. Cloudy white debris within the anterior chamber is consistent with hypopyon in this septic calf.

pressure. Intestinal structures that may ping in a neonate include the abomasum, small intestine, and cecum. Succession of the abdomen is used to evaluate for the presence of excessive fluid in abdominal viscera, including the abomasum, small intestine, cecum, and rumen. The presence of sloshing fluid sounds in the abdomen (succussion splash) is an indication of fluid distension of the viscera caused by decreased intestinal motility and fluid accumulation.
- Characteristics of the diarrhea: patients should be evaluated for color, odor and volume of feces, presence of tenesmus, blood, and mucus.

DIFFERENTIAL DIAGNOSES

- Important differential diagnoses for infectious enteritis can be broadly classified into bacterial, viral, and protozoal. There is a strong correlation between age and the observation of particular pathogens. Common differential diagnoses associated with age in calves and small ruminants are shown in **Table 2**.
- For an in-depth discussion of clostridial enteritis, please see Simpson KM and colleagues' article, "Clostridial Abomasitis and Enteritis in Ruminants," in this issue; nematodiasis can be seen in Craig TM article, "Gastrointestinal Nematodes, Diagnosis and Control," in this issue; coccidiosis can be seen in Keeton STN and Navarre CB's article, "Coccidiosis in Large and Small Ruminants," in this issue; and herd assessment and control of *Salmonella* can be seen in Holschbach CL and Peek SF's article, "Salmonella in Dairy Cattle," in this issue. This article provides an overview of the salient features of the various infectious enteritis diseases in ruminant neonates (less than 6 months of age).

BACTERIAL ENTERITIS
Escherichia coli

Enterotoxigenic Escherichia coli

- Fimbria (pili) confer the ability of ETEC to attach to immature enterocytes. Fimbria antigens identified in pathogens causing disease in livestock include F4 (K88), F5 (K99), F6 (987P), F41, F42, F165, F17, and F18.

Table 2
Timeline for calf diarrhea agents

Agent	Typical Age at Infection	Small Ruminants
E coli (ETEC, K99)	0–7 d	—
E coli (EHEC)	2 d–4 wk	—
Rotavirus	5–14 d	Up to 16 wk; may differ depending on serogroup
Coronavirus	5 d–1 mo	—
Cryptosporidium	1–4 wk	1–4 wk
Clostridium perfringens	Varies with type	Varies with type
Salmonella	5–14 d, anytime	1–7 d, anytime
Giardia	2 wk–2 mo	—
BVDV	First month of life, anytime	—
Nematodiasis	After 3 wk of life	After 3 wk
Coccidia (*Eimeria*)	After 1 mo of life, weaning	2 wk–5 mo, weaning

Abbreviations: BVDV, bovine viral diarrhea virus; EHEC, enterohemorrhagic *E coli*; ETEC, enterotoxigenic *E coli*.

- Enterotoxins produced by ETEC stimulate increased secretion by intestinal crypt cells, causing a severe secretory diarrhea.
- Expression of the enterocyte surface proteins that allow for ETEC pili attachment decreases with age. Thus, affected ruminants are usually less than 7 days of age and often less than 4 days of age.
- Necropsy findings include fluid-filled intestines with a lack of mucosal damage or hemorrhage.
- Diagnosis is through fecal culture followed by immunoassay for the fimbria antigen or polymerase chain reaction (PCR) to detect the specific fimbria virulence factor gene.
- PCR can also be used to identify the specific toxin virulence factor genes.

Attaching and effacing /Shiga toxin–producing, enterohemorrhagic Escherichia coli

- Belong to the "O" labeled serogroups.
- Cause cytotoxic damage to the intestinal mucosa, producing a mucohemorrhagic colitis. Calves experience diarrhea, dysentery, and abdominal pain.
- Clinical signs generally occur in calves 2 days to 4 weeks of age; however adult cattle may have subclinical disease and serve as a source of infection.
- Common necropsy findings include mucosal damage, mucosal petechiation, and GI hemorrhage.
- Diagnosis is through fecal culture followed by PCR for bacterial virulence-associated genes.

Salmonella

- There are many subtypes of Salmonella species. Cattle disease is mainly caused by serogroups B, C, D, and E.
- Infection can result in a wide range of clinical disease, from subclinical shedders to acute bacteremia, endotoxemia, and death.
- The most common clinical signs in young ruminants are fever, diarrhea, anorexia, depression, and dehydration. Affected animals frequently show signs of endotoxemia or sepsis. Infection results in severe inflammation of the mucosa. Rapid emaciation occurs in clinically affected animals because of cachexia stimulated by systemic inflammation coupled with malabsorption and protein loss from the inflamed gut.
- Septic calves require more intensive treatment, including systemic antibiotics.
- Diagnosis is based on fecal culture with increased sensitivity achieved by using an enrichment broth, followed by PCR.
- Necropsy findings usually include fibrinous to fibrinonecrotic enteritis, and there may be signs of bacterial embolization to other organs such as the kidneys.
- Some Salmonella serotypes are zoonotic (eg, Salmonella Typhimurium, Salmonella Newport).[4] Salmonella Dublin is host adapted in cattle, meaning that a nonclinical carrier status can exist in infected cattle.[3]
- For further details, please refer to Holschbach CL and Peek SF's article, "Salmonella in Dairy Cattle," in this issue.

Clostridium perfringens

- Clostridia species are present in the soil and can be cultured from the intestinal tract of normal livestock. Clostridium perfringens proliferates quickly postmortem, making definitive diagnosis difficult. Diagnosis is usually based on history, rapidly progressing clinical signs, necropsy findings, culture results, and the presence of toxins. C perfringens types A, B, C, D, and E can cause abomasitis or enteritis in

young ruminants. **Table 3** lists common diseases caused by each type and the specific toxins produced. The different types produce different toxin profiles, and the actions of these various toxins largely dictate the clinical signs observed.

- *C perfringens* type A causes hemorrhagic abomasitis and enteritis in calves.
- Clinical signs include pasty feces, which may progress to hemorrhagic diarrhea, accompanied by a painful distended abomasum. Clinical signs progress quickly and calves can be found dead without previously observed clinical signs.
- The alpha toxin is a phospholipase that causes endothelial damage, resulting in hemorrhagic and necrotic intestinal lesions. Normal abomasal pH and GI motility reduce the likelihood of clostridial overgrowth. Bacterial proliferation and toxin production are usually associated with decreased abomasal motility and increased abomasal pH.
- *C perfringens* types B and C both cause severe necrotic enterocolitis and enterotoxemia in lambs, kids, calves, piglets, and foals. The disease is characterized by diarrhea that swiftly becomes hemorrhagic and contains sloughed GI mucosa. Systemic signs progress rapidly from weakness, dehydration, and depression to toxemia and death. Progression may be so swift that overt signs of diarrhea may not be observed. Types B and C produce beta toxin, which is highly pathogenic but readily inactivated by proteolytic enzymes present in the intestinal tract, such as trypsin. Neonates are predisposed because of the presence of trypsin inhibitors in colostrum. The disease is generally seen in neonatal ruminants most commonly less than 10 days of age but can occur up to 1 month of age if trypsin inhibitors are still present in the diet. Diagnosis should be suspected based on rapidity and severity of disease, necropsy findings that include severe mucosal ulceration of the small intestine and colon, and identification of the bacteria in intestinal contents. Beta toxin assays are not generally available from diagnostic laboratories in the United States.
- *C perfringens* type D is associated with overeating disease and is most commonly seen in fast-growing lambs and kids. Bottle-raised animals and animals consuming large amounts of readily fermentable carbohydrates are most susceptible. The epsilon toxin may cause local intestinal necrosis but is also absorbed and results in systemic disease related to disruption of endothelial cells in affected organs.
- Please refer to Simpson KM and colleagues', "Clostridial Abomasitis and Enteritis in Ruminants," in this issue.

Table 3 Diseases caused by *Clostridium perfringens*		
C perfringens Type	Toxin Produced	Disease
A	Alpha	• Hemorrhagic enteritis of cattle • Abomasal tympany and ulcers in neonatal calves • Gas gangrene • Yellow lamb disease
B	Alpha, beta, epsilon	• Lamb dysentery • Enterotoxemia (overeating disease) of foals
C	Alpha, beta	• Necrotic hemorrhagic enterotoxemia of calves, lambs, kids, foals, and piglets
D	Alpha, epsilon	• Enterotoxemia of sheep, goats, and cattle
E	Alpha, iota	• Abomasal tympany and ulcers in calves • Enteritis in rabbits

VIRAL ENTERITIS

Rotavirus

- Rotavirus is a common cause of diarrhea in neonatal calves and is often involved in coinfections with other diarrheal pathogens.
- The virus invades small intestine villous epithelial cells, and replicates in the cytoplasm. Infection is usually self-limiting because enterocytes undergo cytolysis faster than they can be replaced by the host. This infection causes intestinal villi to become blunted as villous epithelial cells are replaced by squamous/cuboidal epithelial cells. Small intestinal villus atrophy results in maldigestion and malabsorption.
- Rotavirus also elaborates an enterotoxin, NSP4, which causes calcium influx into the cell resulting in a secretory component to the diarrhea. Damaged epithelial cells also release vasoactive components, increasing permeability and fluid loss. As villous epithelium is lost, hyperplasia of crypt cells with increased secretory capacity also exacerbates the secretory component of diarrhea in these animals.
- Clinical signs are usually seen 1 to 3 days after infection, and can last for 5 to 9 days.
- Adult cows may shed the virus at the time of parturition, facilitating transmission to calves.
- Rotaviral enteritis can be diagnosed by submitting fecal samples for immunofluorescence, electron microscopic examination, or PCR. Other immunoassays exist but may not be readily available for clinical diagnostics. Feces collected early in the disease, during the first 24 to 48 hours, generally have a higher diagnostic value, because signs of diarrhea frequently continue after fecal shedding of viral particles has ceased.

Coronavirus

- Infection by coronavirus can occur via the oral or respiratory route. Corona virus causes 3 clinical syndromes: calf diarrhea, winter dysentery in adult ruminants, and respiratory disease.
- Viral infection begins in the small intestine but can spread to the colon. Viral S protein facilitates attachment and fusion with host cells. Mature villous epithelial cells are the primary target; however, crypt cells can also be affected. The virus replicates within the enterocytes and causes cell lysis. Disease caused by coronavirus is generally more severe than rotaviral enteritis and the disease manifests as a mucohemorrhagic enterocolitis, with clinical signs persisting longer than rotavirus because of crypt cell involvement. As with rotavirus, the loss of villous epithelial cells causes a maldigestive and malabsorptive diarrhea with secondary secretory component from crypt cell proliferation. The maldigestion results in accumulation of undigested lactose causing an osmotic diarrhea.
- Coronavirus can be transmitted to calves by carrier cows with virus shedding increased at parturition and during winter months.
- Diagnosis of coronavirus is through PCR of feces, electron microscopic examination of feces, virus isolation, or immunoassays.

BOVINE VIRAL DIARRHEA

- Diarrhea caused by peracute bovine viral diarrhea virus (BVDV) infection can occur in immunocompetent, non–persistently infected calves.[4]
- Morbidity rates of peracute bovine viral diarrhea (BVD) may reach up to 40% with mortalities reported at 20%.[4]

- Clinical signs associated with peracute BVD include severe diarrhea, pyrexia, thrombocytopenia, hemorrhagic disease, and death.
- Persistently infected calves may have severe enteritis as part of mucosal disease syndrome or may be more susceptible to diarrhea caused by other diarrheal agents because of their immunocompromised status.

Other Viruses

- Other zoonotic viruses that may be associated with diarrhea in calves are Norovirus (bovine Norovirus) and Torovirus (bovine Torovirus [BToV])
- Norovirus is a major cause of acute gastroenteritis in humans; however, the virus isolated from cattle is phylogenetically distinct from human viruses, which may indicate that it has a low zoonotic potential. Experimental infections in newborn calves showed that the virus infects small intestinal epithelial cells causing villous blunting.[5] Norovirus has also been detected in the feces of clinically healthy calves.
- Toroviruses cause acute enteric infection in piglets and children, and BToV has been found in feces of diarrheic calves.[6] It causes a mild to moderate diarrhea in calves less than 3 weeks of age. The virus causes damage to villous and cryptic enterocytes in the upper small intestine. The virus isolated from cattle has antigenic cross reactivity with human toroviruses.
- Many other viruses have been associated with enteric disease in small ruminants, including adenoviruses, astroviruses, bunyaviruses, and paramyxoviruses.[7] However, the relevance of these viruses to clinical practice in North America is unknown.

PARASITIC GASTROENTERITIS
Protozoa

Cryptosporidium

- There are currently 13 species of *Cryptosporidium* with varying degrees of host specificity. Multiple genotypes of *Cryptosporidium parvum* have been identified and can cause enteritis in sheep, goats, and humans.[8] Although it can infect all ages of ruminants, clinical signs are typically seen in preweaning animals. *Cryptosporidium hominis* infects humans, and *Cryptosporidium andersoni* has been found in the abomasum of cattle but its clinical significance is unknown.
- Infection occurs via ingestion of an encysted sporulated oocyst. The parasite invades intestinal epithelium but remains extracytoplasmic, residing in the cell membrane cleft.
- Epithelial destruction causes mild to moderate villous atrophy, resulting in a malabsorptive diarrhea.
- Small infective doses can result in prolonged infection and high parasite burdens because of the phenomenon known as autoinfection, in which the parasite replicates within the host and is directly reinfective without exiting the body.
- The organism is extremely hardy in the environment and is resistant to most chemical disinfectants, including bleach and alcohol. Ammonia-based or peroxide-based products are effective. Care should be taken to avoid contamination of watersheds, which can result in significant environmental and public health issues.
- Diagnosis is through fecal smear or sugar floatation; however, the parasite is very small and may be missed by less experienced technicians. Acid-fast staining of samples increases sensitivity. In areas where acid-fast stain may not be readily

available, there is also a technique for using more typical Ziehl-Neelsen stain to identify *Cryptosporidium* oocysts.[9]

- On-farm control of cryptosporidiosis is difficult because of the extremely high levels of oocytes shed and the environmental hardiness of oocytes resulting in a high environmental burden. The infective dose is small because of the replication and autoinfection that take place within the host.
- Several drugs have been tested and found to have limited activity against *Cryptosporidium*, including paromomycin,[10] decoquinate,[11] and halofuginone. Of these, halofuginone is considered the most promising but is not available or labeled in all countries and has limited efficacy in cases of multipathogen diarrhea complex.[12]

Giardia

- *Giardia duodenalis* (also called *Giardia lamblia*, *Giardia intestinalis*) is classified into different assemblages based on genotypes. Assemblages A and B are zoonotic, and assemblage E is livestock associated.
- All 3 assemblages have been reported in cattle.[8]
- Young calves are most often affected within the first 2 months of life, and infection is often asymptomatic or subclinical. However, giardia infection can cause acute or chronic diarrhea, reduced weight gain, and general ill thrift in young calves. *Giardia* is commonly found in coinfections with coccidia or *Cryptosporidium*.
  ○ Infection occurs via ingestion of cysts from the environment. After ingestion, each cyst releases 2 trophozoites in the upper small intestine. The trophozoites can either attach to epithelial cells via their ventral disk or live freely in the intestinal lumen. Trophozoites multiply in the lumen by binary fission.
  ○ Exposure to bile salts causes encystation.
  ○ Excreted cysts are immediately infective (entire cycle in humans, 72 hours).
  ○ The prepatent period in ruminants ranges from 3 to 10 days.
- Diagnosis is through fecal smear or floatation; however, fecal examination for *Giardia* requires relevant expertise. Diagnosis can also be achieved by antigen detection in feces via indirect fluorescent antibody test, enzyme-linked immunosorbent assay, or SNAP test, or by PCR. In areas where diagnostic laboratories are difficult to access, staining fecal smears with a Romanowsky stain can aid in identifying organisms.[13]

Coccidiosis

- Coccidia are fairly host specific, and most do not cause clinically relevant disease. Ruminants are affected by species of the genus *Eimeria*. At least 13 *Eimeria* species infect cattle, 16 infect sheep, and 15 have been reported in goats. Only a few *Eimeria* species are pathogenic and cause significant disease. In cattle, life-threatening disease is most commonly caused by *Eimeria bovis* and *Eimeria zuernii*.[14]
- Infected animals shed unsporulated oocysts, which sporulate in the environment to become infective. Oocysts are resistant to environmental changes and persist, especially in cool, moist environments. Once ingested, the oocysts are degraded to allow excystation to occur. Schizonts and gamonts replicate within cells of the lower ileum, cecum, and large intestine, rupturing the host cells.
- The life cycle length differs depending on species, but in general the prepatent period ranges from 15 to 20 days.

- Disease is usually seen in older calves, kids, and lambs, and is usually associated with a stressor such as weaning.
- Typical clinical signs are diarrhea with tenesmus. Mucus and blood may be observed in the feces. In some cases, severe bloody diarrhea is a significant cause of blood loss. Neurologic signs (nervous coccidiosis) are also possible and are associated with toxin production by the coccidia in the GI tract.
- Animals raised in contaminated environments can experience chronic reinfections.
- Chronic subclinical infections can present as ill thrift and poorly growing juvenile animals that are susceptible to other diseases. These animals may also show anemia and hypoproteinemia.
- Diagnosis is through fecal floatation, McMaster, or modified Stoll techniques.

For detailed information, please refer to Keeton STN and Navarre CB's article, "Coccidiosis in Large and Small Ruminants," in this issue.

NONINFECTIOUS DIFFERENTIAL DIAGNOSES FOR ENTERITIS

Differential diagnoses of noninfectious causes of diarrhea in neonatal and juvenile ruminants include the following:

- Improper mixing of milk replacer
- Improper handling of milk or milk replacer
- Grain overload (lactic acidosis)

DIAGNOSTICS

Laboratory diagnostic tests are important for guiding therapy, but they are poor predictors of prognosis in calves with diarrhea.[15] Physical examination findings are more sensitive predictors of outcome and should be the primary consideration when making clinical decisions.[15]

Packed Cell Volume and Serum Total Protein

- Packed cell volume (PCV) and serum total protein (STP) aid in the assessment of the level of anemia and hypoproteinemia, respectively. PCV and STP can be determined using a hematocrit centrifuge and refractometer.
- Assessment of these parameters is useful in guiding the initiation and continuation of fluid therapy. Increased PCV and STP levels generally indicate dehydration at the time of initial presentation. However, PCV and STP levels decrease in severely dehydrated neonates treated with large volumes of intravenous fluids and can be detrimental to the survival of the patient if not monitored so that fluid therapy can be adjusted appropriately.
- Low STP level is associated with protein loss via the GI tract or failure of passive transfer of immunity in neonatal animals. In cases of infectious enteritis, low hematocrit can be caused by blood loss from the GI tract or anemia of chronic disease. In cases of blood loss from the GI tract, both hematocrit and STP are decreased simultaneously. Coccidiosis is a frequent cause of whole-blood loss via the GI tract. Diarrheal diseases also causing blood loss in neonates include salmonellosis, enterohemorrhagic E coli, and clostridial enteritis.

Blood Gas Analysis

- Blood gas analysis provides an assessment of blood pH and acid/base status. Metabolic acidosis is common in neonatal and juvenile ruminants with enteritis.

Debilitated animals who are not ventilating adequately because of weakness may also have evidence of respiratory acidosis. Portable point-of-care blood analyzers (i-STAT, epoc) are available for use in ruminants and can perform blood gas analysis.

- These blood analyzers frequently include major electrolytes in their analysis, allowing assessment of potassium, sodium, and chloride status. In acidotic patients, it is important to consider the extracellular shift of potassium when assessing blood potassium levels. Hyperkalemia may be observed in patients with metabolic acidosis, increasing the risk of cardiac arrhythmias and potential cardiac arrest. Hyperkalemia generally resolves on initiation of appropriate fluid therapy.
- Blood lactate levels can be helpful in assessing systemic perfusion. Severely dehydrated calves can have markedly increased blood L-lactate levels. Note that most lactate analyzers only report L-lactate and not D-lactate. D-Lactate is produced by microbial flora in the colon and is exacerbated in conditions resulting in maldigestion and malabsorption. D-Lactate is an important cause of metabolic acidosis in calves with enteritis and contributes to the weakness and decreased mentation often observed in these patients.[16]

Complete Blood Count and Serum Biochemical Analysis

- A complete blood count provides information to appropriately classify the anemia present (smear evaluation) and assess inflammation (leukocytes with differential counts, and fibrinogen).
- Leukopenia characterized by neutropenia with a left shift, and the presence of cellular toxic changes are evidence of systemic sepsis and might be the result of systemic endotoxemia, bacteremia, or salmonellosis.
- Leukopenia and thrombocytopenia may be observed with acute BVDV type II infection. Marked leukopenia may also be observed with BVDV mucosal disease.
- Serum biochemical analysis assesses concentrations of albumin and globulin, identifies electrolyte derangements, and provides evidence of organ dysfunction secondary to the infectious agent.
- Portable serum biochemical analyzers may be useful in identifying electrolyte imbalances but may not be equipped to assess albumin, globulin, and organ enzyme activities.

TREATMENT
Principles of Treatment of Infectious Enteritis in Neonatal Ruminants

Infectious enteritis causes diarrhea and associated fluid and electrolyte losses. Thus, fluid therapy is an important part of management of infectious enteritis. Oral fluid therapy, if instituted early in the disease process, can be highly successful and cost-effective in treating animals with enteritis and diarrhea. Oral electrolyte solutions should be evaluated for their sodium composition, pH buffering capacity, energy content, and osmolarity.[3] Guidelines for electrolyte replacers are provided in **Table 4**.

In animals with severely compromised intestinal motility, intravenous fluid therapy can be more effective at correcting the electrolyte imbalances and fluid loss than oral administration. Physical examination findings and diagnostic results should be used to guide treatment decisions, and some published algorithms exist to help clinicians in the decision process.[17] Blood and protein loss should also be considered and treated accordingly. Please refer to the March, 2009 issue for an in-depth discussion of fluid therapy in calves.

Table 4
Recommendations for electrolyte, carbohydrate, buffering capacity, and osmolality of oral electrolyte replacement fluids used to treat enteritis and diarrhea in neonatal ruminants

Component	Recommendation
Na^+ concentration	90–130 mEq/L
K^+ concentration	10–30 mEq/L
Cl^- concentration	40–80 mEq/L
Glucose + glycine concentration	100–280 mM/L
Buffering capacity (SID = $[Na^+] + [K^+] - [Cl^-]$)	50–80 mEq/L
[Glucose + glycine]/[Na] ratio	1:1–3:1
Total osmolality	400–600

Abbreviation: SID, strong ion difference, measured.

Intravenous Crystalloid Fluids

- These include 1.3% sodium bicarbonate, 0.9% sodium chloride, and balanced electrolyte solutions such as lactated Ringer or Plasma-Lyte.
- The choice of the crystalloids may depend on the test results of a serum biochemical analysis.
- When serum biochemical analysis test results are not available, a balanced electrolyte solution such as lactated Ringer or Plasma-Lyte should be considered for intravenous fluids.
- Both the level of dehydration at presentation and ongoing fluid losses caused by diarrhea must be considered when calculating fluid administration rates. Administration rates greater than maintenance are often necessary to treat hypovolemic shock caused by dehydration and account for continued losses from diarrhea. The patient's STP status must also be considered. Intravenous fluids should be administered with caution in patients with albumin levels less than 2 g/dL.
- Initial treatment of shock with intravenous fluid replacement may be indicated in severely compromised patients. A typical shock fluid therapy plan is to provide 90 mL/kg of intravenous fluids at a maximum rate of 40 to 50 mL/kg/h.[18] Slower rates should be used for small ruminants and in animals with low total protein levels. Signs of appropriate response include improved mentation and activity, decreased skin tent or eyeball recession, improved suckle response, decreased capillary refill time, and improved peripheral perfusion noted by warming of distal extremities. Signs of fluid overload include wet cough, harsh lung sounds, increased respiratory rate, and edema.
- General maintenance fluid rates for juvenile ruminants range from 4 to 6 mL/kg/h (100–150 mL/kg/d). Additional fluid losses from diarrhea may increase fluid needs by 50% to 100%. Thus, total fluid rates in ruminants with active diarrhea are in the range of 1.5 to 2 times maintenance. Any oral fluid administration also contributes to the daily fluid requirement and should be taken into account when calculating fluid volume to correct dehydration and when calculating maintenance requirements.
- Most neonates with enteritis have decreased nutritional intake and absorption. They benefit from additional intravenous dextrose supplementation. Dextrose may safely be added to intravenous fluids at a concentration of 2.5% to 5% when administered at a maintenance fluid rate. This concentration should be decreased proportionally when increasing fluid rate to more than

maintenance, or if blood glucose measurements are greater than the normal range (6.5 ± 1.2 mmol/L, 117 ± 21.6 mg/dL).[19,20] Note that neonatal ruminants are effectively monogastrics and normally have higher blood glucose levels than adults, so adult reference ranges should not be applied to them. A reasonable goal for blood glucose management in calves is to keep blood glucose within 80 to 120 mg/dL.

- Correction of hyperkalemia can be accomplished by administering small volumes of hypertonic (8.4%) sodium bicarbonate, followed by oral electrolytes.[21] Hypertonic sodium bicarbonate can safely be administered at a rate of 6.4 mL/kg body weight (equivalent to 6.4 mEq HCO_3^-/kg body weight) as a bolus over 5 minutes in calves with diarrhea and evidence of metabolic acidosis.
- A recent issue (March, 2009) covered fluid therapy in calves extensively.

Colloids

- Plasma transfusion should be considered in ruminants with severe hypoproteinemia (albumin levels <1.5 g/dL) on serum biochemical analysis.
- Dosage rates for plasma administration range from 10 to 20 mL/kg.[22]
- Blood transfusion (particularly in coccidiosis) should be considered when PCV is less than 12%[22] with associated clinical signs of compromise, including tachycardia, tachypnea, weakness, and poor appetite.
- Following plasma or blood transfusion administration, fluid therapy may be continued with crystalloid fluids.

Antimicrobial and Nonsteroidal Antiinflammatory Therapy

- Enteritis can predispose neonates to bacteremia and secondary infections because of compromised gut barrier and bacterial translocation.
- Broad-spectrum antibiotics, with special attention to adequate gram-negative coverage, should be instituted in patients showing signs of endotoxemia or sepsis. Although the choice of antibiotics should be based on susceptibility of the isolate cultured, broad-spectrum antibiotics may be initiated while awaiting these results. Susceptibility of *Salmonella* to tetracyclines, ampicillin, and amoxicillin is variable, whereas resistance to penicillin, erythromycin, and tylosin is highly likely.[23] Florfenicol should be considered for treatment of salmonellosis.[23] Use of aminoglycosides should be avoided because of prolonged tissue residues in animals intended for food. Cephalosporins and fluoroquinolones may not be used in an extralabel manner in the United States. Tetracyclines should be avoided in dehydrated neonates until fluid hydration and renal perfusion are restored to minimize the risk of nephrotoxicity.
- Use of nonsteroidal antiinflammatory drugs (NSAIDs; eg, flunixin meglumine) may be considered to control pyrexia and inflammation. Flunixin meglumine (1.1 mg/kg intravenously) or meloxicam (0.5 mg/kg intravenously or subcutaneously) were reported to improve outcome in calves with nonspecific diarrhea.[24,25] The use of NSAIDs should be restricted in dehydrated ruminants and only administered once the patient has been sufficiently hydrated.
- Metaphylactic use of antimicrobials can only be recommended for outbreaks caused by a specific bacterial pathogen. Prophylactic treatment with antimicrobials has been shown to increase the risk of diarrhea in neonatal calves.[26]

Prevention

- Appropriate colostrum handling and administration are instrumental in preventing neonatal diarrhea in ruminants. Few clinicians dispute a link between

inadequate colostrum consumption and an increased risk for diarrhea in neo-nates. Supplementing calves with colostrum orally past the traditional 24 hours after birth decreases diarrhea and diarrheal treatments in preweaned calves[26,27]

- A minimum of 150 to 200 g of immunoglobulin G (IgG) in colostrum or a colostrum replacer should be fed to calves within the first 24 hours (Chigerwe and colleagues, 2008)[28] to provide adequate transfer of passive immunity. The concentration of IgG in colostrum can be estimated before feeding calves using a hydrometer or a Brix refractometer.
- Evaluation of the passive transfer status of neonates provides valuable risk assessment, husbandry, and epidemiologic information in both individual cases and herd outbreaks. Passive transfer status can be assessed using STP, sodium sulfite precipitation, immunocrit test, or radial immunodiffusion.
- Other factors associated with an increased risk of diarrhea include hygiene of the maternity area and neonate housing, stocking density, and disinfection practices. Attention should be paid to maternal health prepartum as well.
- Vaccination of the dams before parturition with a K99 *E coli*, rotavirus, coronavirus product can reduce the diarrhea associated with that pathogen.[29,30] Vaccination for other diarrheal agents is of varying efficacy.
- In beef operations, a method known as the Sandhills Calving System can be used to prevent calf diarrhea in a herd or to break a herd of a recurring neonatal diarrhea problem.[31] In this method, cows are continually calving on new ground, reducing contamination and reducing mixing of calves of different ages.

SUMMARY

Causes of infectious enteritis in adult ruminants are bacterial, viral, and parasitic. The most consistent clinical sign of infectious enteritis is diarrhea. Specific causes of infectious enteritis in adult ruminants cannot be distinguished easily based on clinical examination alone. Laboratory diagnostic tests are required to differentiate the causes. Most of the causes have herd implications, thus identification of the cause is recommended. Management of infectious enteritis in adult ruminants includes administration of oral electrolyte fluids or intravenous fluids such as crystalloids and colloids, NSAIDs, antibiotics, anthelmintics, and anticoccidiosis treatments.

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