DİARRHEA İN NEONATAL RUMİNANTS

Several enteropathogens are associated with diarrhea in neonates. Their relative prevalence varies geographically, but the most prevalent infections in most areas are *Escherichia coli*, rotavirus, coronavirus, and *Cryptosporidium parvum*.

Cases of neonatal diarrhea are commonly associated with more than one of these agents, and the cause of most outbreaks is multifactorial.

Determining the particular agents associated with an outbreak of diarrhea can be important, because specific therapy and prophylaxis are available for some. Also, some agents have zoonotic risk. Diarrhea is also present in septicemic colibacillosis.

BACTERIA:

E coli is the most important bacterial cause of diarrhea in calves during the first week of life; at least two distinct types of diarrheal disease are produced by different strains of this organism.

One type is associated with enterotoxigenic *E coli*, which has two virulence factors associated with production of diarrhea. Fimbrial antigens enable them to attach to and colonize the villi of the small intestine of neonatal calves in the first days of life

Strains in calves most commonly possess K99 (F5) or F41 fimbrial antigens, or both. These antigens are the focus of immunologic protection.

Enterotoxigenic *E coli* also elaborate a thermostable, nonantigenic enterotoxin (Sta) that influences intestinal ion and fluid secretion to produce a noninflammatory secretory diarrhea

Diarrhea in calves and lambs also has been associated with enteropathogenic *E coli* that adhere to the intestine to produce so-called attaching and effacing lesions, with dissolution of the brush border and loss of microvillous structure at the site of attachment, a decrease in enzyme activity, and changes in ion transport in the intestine.

These enteropathogens are also called "attaching and effacing *E coli*." Some produce verotoxin, which may be associated with a more severe hemorrhagic diarrhea. The infection most frequently is in the cecum and colon, but the distal small intestine can also be affected. The damage in severe infections can result in edema and mucosal erosions and ulceration, leading to hemorrhage into the intestinal lumen.

SALMONELLA SPP

Salmonella spp, especially *S* Typhimurium and *S* Dublin, but occasionally other serovars, cause diarrhea in calves 2–12 wk old.

Salmonellae produce enterotoxins but are also invasive and produce inflammatory change within the intestine. In calves, infection commonly progresses to a bacteremia.

CLOSTRIDIUM PERFRINGENS

Clostridium perfringens types A, B, C, and E produce a variety of necrotizing toxins and cause a rapidly fatal hemorrhagic enteritis in calves.

The disease in calves is rare and usually sporadic. Infection with type B or C is a common cause of enteritis and dysentery in lambs.

CAMPYLOBACTER JEJUNI

Campylobacter jejuni and *Yersinia enterocolitica* may be present in the feces of calves and lambs with diarrhea but also may be found in the feces of healthy animals.

VİRUSES:

Rotavirus is the most common viral cause of diarrhea in calves and lambs. Groups A and B rotavirus are involved, but group A is most prevalent and clinically important and contains several serotypes of differing virulence.

Rotavirus replicates in the mature absorptive and enzyme-producing enterocytes on the villi of the small intestine, leading to rupture and sloughing of the enterocytes with release of virus to infect adjacent cells.

Rotavirus does not infect the immature cells of the crypts. With virulent strains of rotavirus, the loss of enterocytes exceeds the ability of the intestinal crypts to replace them; hence, villous height is reduced, with a consequent decrease in intestinal absorptive surface area and intestinal digestive enzyme activity.

CORONAVIRUS

Coronavirus is also commonly associated with diarrhea in calves. It replicates in the epithelium of the upper respiratory tract and in the enterocytes of the intestine, where it produces similar lesions to rotavirus but also infects the epithelial cells of the large intestine to produce atrophy of the colonic ridges.

Other viruses, including Breda virus (torovirus), a calici-like virus, astrovirus, and parvovirus, have been demonstrated in the feces of calves with diarrhea and can produce diarrhea in calves experimentally.

However, these agents have also been found in the feces of healthy calves. The importance of these agents in the syndrome of diarrhea in neonates has yet to be determined.

The viruses of bovine virus diarrhea and infectious bovine rhinotracheitis are reported to cause calf diarrhea, but this is not a common manifestation of these infections.

PROTOZOA:

Cryptosporidium parvum is a common cause of diarrhea in calves and lambs. The parasite does not invade but adheres to the apical surface of enterocytes in the distal small intestine and the colon.

This results in loss of microvilli, decreased mucosal enzyme activity with villous blunting and fusion (leading to a reduced villous surface absorptive area), and inflammatory changes in the submucosa. Mammalian cryptosporidia lack host specificity.

EPİDEMİOLOGY AND TRANSMİSSİON:

Enteropathogens associated with diarrhea are commonly found in the feces of healthy calves; whether intestinal infection leads to diarrhea depends on a number of determinants, including differences in virulence of different strains of a pathogen and the presence of more than one pathogen.

The resistance of the calf is of major importance and is largely determined by successful passive transfer of colostral immunoglobulins.

Colostrum-deprived calves are highly susceptible to infection with enteropathogens and develop severe and often fatal disease.

- The progression of infection, the severity of lesions produced, and the severity of the diarrhea can be modulated by immunoglobulins received via colostrum.

- Immunoglobulins act directly on pathogens in the intestinal lumen during the period of colostrum ingestion as well as after, because significant amounts of circulating immunoglobulins are resecreted into the intestine, especially when the concentration of circulating immunoglobulin is high.

- The lack of specific antibodies in dams that have not been exposed to specific pathogens, and the use of specific vaccines, further modulate this influence. Stress caused by a poor environment, inadequate protection from the weather, or an insufficient or inappropriate diet also increases the risk of disease.

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Diarrhea in neonatal ruminants is usually associated with disease of the small intestine and can be caused by hypersecretion or malabsorption. Hypersecretory diarrhea develops when an abnormal amount of fluid is secreted into the gut, exceeding the resorptive capacity of the mucosa.

In malabsorptive diarrhea, the capacity of the mucosa to absorb fluid and nutrients is impaired to the extent that it cannot keep up with the normal influx of ingested and secreted fluids.

This is usually the result of villous atrophy, in which the loss of mature enterocytes at the tips of the villi results both in a decrease in villous height (with a consequent decrease in the surface area for absorption) and in loss of the brush border digestive enzymes.

The extent and distribution of villous atrophy varies with different pathogens and can explain variation in the severity of clinical disease.

Malabsorptive diarrhea may be aggravated by the colonic fermentation of nutrients that normally would have been absorbed in the small intestine.

Fermentation products, especially lactic acid, appear to draw water into the colon osmotically, which contributes to the severity of diarrhea.

Inflammation contributes to the pathophysiology of diarrhea in most intestinal infections, and mediators of inflammation can affect ion flux within the intestine. Inflammation also leads to vascular and lymphatic damage and to structural damage of the crypt-villus unit.

Most infectious forms of diarrhea have hypersecretory, inflammatory, and malabsorptive components, although one usually predominates.

These lead to a net loss of water, sodium, potassium, and bicarbonate; if severe, the calf develops hypovolemia, hyponatremia, acidemia, and prerenal azotemia.

Enterotoxigenic *E coli* produce the enterotoxin Sta, which stimulates marked hypersecretion by activating guanylate cyclase and by inducing a net secretion of sodium and chlorine. The membrane-bound sodium-glucose cotransport system remains functional but cannot compensate for the increased secretory activity.

Salmonellae also elaborate enterotoxins. Inflammation, leading to necrosis of the enterocyte, submucosal inflammatory infiltration, and villous atrophy, is also a major component of the pathophysiology of diarrhea produced by salmonellae, as well as of diarrhea produced by enteropathogenic *E coli* and by toxigenic C *perfringens*. Infections with verotoxin-producing enteropathogenic *E coli* result in accumulation of fluid within the large intestine and extensive damage to the large intestinal mucosa, with edema, hemorrhage, and erosion and ulceration of the mucosa, which results in blood and mucus in the lumen.

Viruses usually produce a malabsorptive diarrhea by destroying the absorptive cells of the mucosa, thus shortening the intestinal villi. The mechanism by which cryptosporidia produce diarrhea is not completely understood, but it appears to have both malabsorptive and inflammatory components.

- Inappropriately formulated milk replacers produce diarrhea by two mechanisms, both associated with malabsorption.
- Vegetable (especially soybean) products are commonly used as protein sources in the manufacture of milk replacers.
- Depending on the degree of refinement, these products may contain carbohydrates that are indigestible in young calves.
- Such carbohydrates are not absorbed in the small intestine and may contribute to diarrhea via colonic fermentation. In addition, most calves <3 wk old appear to have an allergic reaction to soy proteins that results in villous atrophy, leading to diarrhea that is probably malabsorptive.

The major signs are diarrhea, dehydration, profound weakness, and death within one to several days of onset.

Diarrhea due to enterotoxigenic (K99-bearing) *E coli* is seen in calves <3–5 days old, rarely later. However, the age of susceptibility may be extended in the presence of other pathogens. Onset is sudden.

Profuse amounts of liquid feces are passed, and the calves rapidly become depressed and recumbent. Calves may lose >12% of body weight in fluid, and hypovolemic shock and death may occur in 12–24 hr. Body temperature may be increased but is commonly normal or subnormal.

If fluid and electrolyte therapy is administered early, response is usually good. Disease produced by attaching and effacing *E coli* is seen predominantly in calves from 4 days to 2 mo old and may manifest with diarrhea or primarily as dysentery with blood and mucus in the feces. The clinical course is short.

Diarrhea due to *Salmonella* spp usually is not seen in calves <14 days old. It is characterized by feces that are foul smelling and contain blood, fibrin, and copious amounts of mucus. Septicemia, with high fever and depression progressing to prostration and coma, is the salient manifestation of salmonellosis in calves and, although diarrhea is present, death is usually from septicemic rather than from hypovolemic shock. Calves with salmonellosis usually lose weight rapidly and often die despite vigorous therapy.

Hemorrhagic enterotoxemia due to C *perfringens* type B or C is characterized by acute onset of depression, weakness, bloody diarrhea, abdominal pain, and death within a few hours. It usually develops in vigorous calves just a few days old that have large appetites and a ready source of milk. Calves affected with C *perfringens* usually die before treatment can be instituted.