PARTURIENT PARESIS IN SHEEP AND GOATS (MILK FEVER, HYPOCALCEMIA)

- Parturient paresis is caused by a decrease in calcium intake under conditions of increased calcium requirements, usually during late gestation.
- Parturient paresis can occur at any time from 6 wk before to 10 wk after parturition
- Examples of forages with low calcium levels include cereal hays or pasture, poor-quality grassy hays and pasture, and corn silage.
- Most grains also contain little calcium but additionally have high levels of phosphorus, causing an inverse calcium:phosphorus ratio, increasing dietary risk.
- Vitamin D deficiency, which occurs in housed ruminants during winter months, also depresses calcium absorption from the GI tract.

CLINICAL FINDINGS AND DIAGNOSIS

- Characteristically, parturient paresis occurs in outbreaks, with most cases occurring in the last few weeks of gestation, although it is not uncommon for individual animals to be affected.

- he onset is sudden and often follows—within 24 hr—an abrupt change of feed, a sudden change in weather, or short periods of fasting imposed by circumstances such as shearing or transportation

- Stiff gait
- Ataxia
- Salivation
- Constipation
- Depressed rumen motility
- Progressing to hyposensitivity
- Bloat
- Recumbency loss of anal reflex and, if untreated, death.

- A working diagnosis is based on the history and clinical signs. A tentative diagnosis of acute hypocalcemia is supported by a dramatic and usually lasting response to slow IV administration of calcium
- Diagnosis can be confirmed by testing serum calcium levels before treatment.
- Urine ketone or serum β-hydroxybutyrate levels should always be evaluated at the same time.
- Hypocalcemia is often classified as total serum calcium levels <2 mmol/L or, if expressed as ionized calcium, <1.1 mmol/L. Normal values are reported as 2.8–3.2 mmol/L for sheep and 2.2–3.05 mmol/L for goats. (To convert from mmol/L to mg/dL, divide the value by 0.25.)
- Animals with low serum albumin, such as occurs with Johne's disease and clinical GI parasitism, may have low total serum calcium and normal ionized calcium.

TREATMENT AND PREVENTION

- Calcium borogluconate IV (50–150 mL of a 23% solution). Calcium-containing products that also contain phosphorus and magnesium, as well as dextrose, likely have additional therapeutic value.
- Oral or SC administration of a calcium solution helps to prevent relapse.
- During treatment, the heart should be monitored, and therapy slowed or stopped if arrhythmias occur.
- For ease of IV administration, it may be preferred to increase the volume of the product by adding 50–150 mL of a 23% calcium borogluconate or gluconate solution to 1 L of a 5% dextrose solution and administering this volume over 10 min.
- Dietary modifications to increase the calcium:phosphorus ratio (>1.5:1) and ensure total calcium in the diet meets NRC requirements (see Table: Calcium Requirements of a Meat Ewe and Dairy Doe During Gestation and Lactation), as well as vitamin D levels, may help to prevent further cases in pregnant animals. Sudden dietary changes or other stressors should be avoided during late gestation, and risk factors for pregnancy toxemia investigated.

TRANSPORT TETANY

- Transport tetany occurs after the stress of **prolonged transport**, typically in cows and ewes in late pregnancy.
- **Crowded, hot, poorly ventilated transport vehicles** (railroad cars or trailers) with minimal or **no access to feed or water appear** to predispose animals to the condition; however, prolonged travel by foot is also a risk factor

- The disease is characterized by recumbency, GI stasis, and coma, and is generally fatal.
- Risk factors include heavy feeding before shipment, deprivation of feed and water for >24 hr during transit, and unrestricted access to water and exercise immediately after arrival.
- Exposure to hot environmental conditions is also associated with an increased incidence
- Hypomagnesemia may be a precipitating factor in cattle and a contributing factor in sheep.

- Clinical signs in cattle may occur while in transit or as long as 48 hr after arrival
- Early clinical signs include restlessness and excitement, trismus, and grinding of teeth
- A staggering gait may be seen, and later, if recumbent, cattle often demonstrate paddling of the hindlegs. Rumen hypomotility and GI stasis are seen, and animals become completely anorectic
- Tachycardia and rapid, labored respiration may develop. Abortion may be a complication.
- Moderate hypocalcemia and hypophosphatemia may be seen in cattle. Some sheep are hypocalcemic and hypomagnesemic, but others show no measurable biochemical abnormalities.

- Some animals respond to treatment with combinations of parenteral **calcium**, **magnesium**, and glucose. IV injections of calcium borogluconate (25% solution at 400–800 mL/cow or 100 mL/ewe) or calcium borogluconate with magnesium sulfate (5% solution, same volumes) can be administered slowly.
- A dose of 50 mL/day can be given SC to affected lambs in feedlots. Repeated injections may be warranted, but failure to respond is common (50%) and most likely due to concurrent muscle necrosis.
- Additional treatment considerations include IV administration of large volumes of polyionic fluids such as lactated Ringer's solution.
- Animals should be offered good quality feeds (eg, alfalfa hay), fresh water, and soft bedding with good footing underneath.
- Sedation may be necessary if animals are hyperexcitable or convulsing.

EQUINE METABOLIC SYNDROME
(INSULIN DYSREGULATİON SYNDROME, EQUINE SYNDROME X, PERİPHERAL CUSHİNG DISEASE)

- Equine metabolic syndrome (EMS) describes a characteristic collection of clinical signs and clinicopathologic changes in equids. It is found in both horses and ponies and has also been recognized in donkeys
- EMS develops in horses 5–16 yr old.
- Breeds most commonly affected include ponies, Saddlebred, Tennessee Walking, Paso Fino, Morgan, Mustang, and Quarter horses.
- Thoroughbreds and Standardbreds infrequently develop EMS. There is no recognized sex predilection.

Etiology and Pathogenesis

- The underlying reason why some horses develop EMS and others do not is not known.
- There appears to be a genetic disposition, both within and between breeds.
- Affected horses may possess a "thrifty" gene that enabled their ancestors to survive in harsh environments. This increased efficiency of energy metabolism became maladaptive in modern environments with plentiful, nutrient-dense feedstuffs.
- The common denominators behind many of the signs associated with EMS appear to be **increased adiposity, insulin resistance**, and **hyperinsulemia**.
- When obesity develops, adipose tissues elaborate leptin and other adipokines as well as tumor necrosis factor and other inflammatory mediators. Increased fat stores in the liver may also predispose to insulin resistance due to down-regulation of insulin receptors.

- Experimentally, **high blood insulin levels** lead to **laminitis** in horses and ponies.
- Insulin has vasoregulatory actions.
- **Insulin resistance** can decrease nitric oxide production and promote **vasoconstriction**.
- **Altered glucose and insulin** levels may also lead to altered epidermal cell function and glucose uptake by epidermal laminar cells. These effects predispose horses with EMS to develop **laminitis**.

Clinical Findings

- There is no clinical picture that is pathognomonic for insulin resistance.
- Horses may exhibit all the phenotypic characteristics of EMS with normal responses to evocative testing.
- Affected horses typically are **obese** with a body condition score >6 out of 9. Even if the overall condition score is not extremely high, there is increased fat deposition in the neck, leading to a "cresty" appearance

- **Fat deposition** over the ribs and over the top line to the tail head is also common.
- **Laminitis** is a common finding. Horses brought in for evaluation with no previous history of laminitis often show evidence of prior episodes such as abnormal hoof growth rings and radiographic evidence of third phalanx rotation or pedal osteitis.
- Laminitis may occur secondary to ingestion of feeds high in soluble carbohydrates, either in the form of lush pasture or high-carbohydrate hays and supplements.

- Horses with EMS may not lose weight without extreme feed restriction; owners commonly report that affected horses remain obese even when fed minimal amounts.
- Obesity may be exacerbated by laminitis, which may limit exercise. Horses appear to have increased appetites and often will eat continually as long as feed is available. Infertility and abnormal reproductive cycles occur in mares affected with EMS.

Diagnosis

- Diagnostic testing for EMS should concentrate on documenting insulin resistance while excluding PPID.
- The presence of obesity and the cresty neck phenotype is not sufficient to make a diagnosis.
- A careful dietary history and physical examination are essential.
- Establishing baseline body condition score and neck circumference will enable assessment of the horse's response to treatment
- Because many conditions, including diet, pain, and stress, can affect blood glucose and insulin levels, diagnostic testing should be performed in a controlled manner in a low-stress environment.
- If the horse has laminitis, diagnostic testing should be delayed until the feet have stabilized and are relatively pain free.

- Insulin should be determined after the horse has been fasted for 6–8 hr. This can be done by leaving only one flake of hay with the horse after 10 PM the night before and then collecting the blood sample the next morning. If those conditions are met, a blood insulin concentration >20 μU/mL is suggestive of insulin resistance.
- The OST is performed by fasting the horse for 6–8 hr and then giving an oral dose of corn syrup at 0.15 mL/kg. Blood should be collected at 60 or 90 min after administration of the corn syrup for insulin determination.
- An **insulin concentration >60 mU/L is abnormal**.

Treatment and Prevention

- Treatment for EMS involves **dietary management** and, if diet and exercise is not sufficient to treat the condition, **medical therapy.**
- Dietary carbohydrate restriction is essential to decrease glycemic and insulinemic response; total calorie intake is restricted to reduce body weight. Pasture access should be eliminated or severely restricted. Use of a grazing muzzle may aid in decreasing pasture ingestion.
- Nonstructural carbohydrate (NSC) should comprise <10% of the hay dry matter, and it should never exceed 16%.
- Horses should initially be fed 1.5% of their ideal body weight in forage per day. This amount can be lowered to 1.25% and then to 1% of ideal body weight after 30 days,

- The **thyroid hormone thyroxine**, in the form of levothyroxine sodium, will accelerate weight loss and thereby improve insulin sensitivity when combined with dietary interventions in horses.
- Horses weighing >350 kg can be given 48 mg/day, PO; smaller horses and ponies should receive 24 mg/day, PO.
- Treatment periods of 3–6 mo are often needed to achieve desirable weight loss

- **Metformin** is poorly absorbed in equids but may decrease postprandial glucose and insulin levels.
- It may lead to improvement in hyperinsulinemic horses at a dosage of 30 mg/kg, PO, tid or bid. It should be given 30 min before a meal if possible.
- However, the longterm efficacy and safety of metformin has not been established in horses. If it is used, blood glucose should be carefully monitored. Use of metformin should be discontinued if hypoglycemia is documented.

ACUTE RUMEN ACIDOSIS

- **Acute rumen acidosis** represents the most severe form of indigestion and is associated with overingestion of rapidly fermentable concentrate feed or the sudden change to a diet containing higher levels of finely ground, rapidly fermentable feeds such as corn or wheat.

- This is less often a herd problem in dairy cattle, but it has occurred when owners have run out of one type of feed and quickly changed to another.

- Sudden introduction of highly fermentable small grain silage into the herd can also result in lactic acidosis (both D and L forms).
- Ruminal acidosis may also occur when cattle are fed grain-based silage that has fermented for less than 2 weeks.
- Another problem that can lead to ruminal lactic acidosis in modern dairy manage- ment systems is improper mixing of TMRs. In these cases, equipment failure or human error can lead to stratification of feedstuffs used in the TMR, and cows at one end of the feed line receive mostly roughage, but those at the other end receive mostly high-sugar, high-starch concentrate.

- **….Within** 6 hours of ingestion, the easily fermentable and high-sugar, high-starch concentrate is broken down to volatile fatty acids and both D- and L-lactic acid.
- Most of this occurs in the rumen, although substantial production of D-lactic acid may also occur in the lower GI tract. The L isomer can be used rapidly, but the D isomer persists and results in D-lactic acidosis.

- ***Streptococcus bovis*** is one of several organisms responsible for the excessive lactic acid production. As more and more lactic and volatile acids are produced, the pH of the rumen contents decreases further into the acid range.
- If sufficient rapidly fermentable starch substrate is available, the rumen pH may decrease to 4.5 to 5.0, destroying most microbes other than *S. bovis*. With very high lactate and histamine content, rumen stasis occurs. *S. bovis* continues to survive at this low pH and perpetuates the problem by producing more lactic acid.

- Rapid accumulation of acids osmotically draws water into the rumen, dehydrating the cow and increasing systemic production of L-lactate from enhanced anaerobic metabolism.
- In addition, the chemical or acid rumenitis damages the rumen mucosa, allowing plasma transudation into the rumen and endotoxin and bacteria escape into the portal circulation.

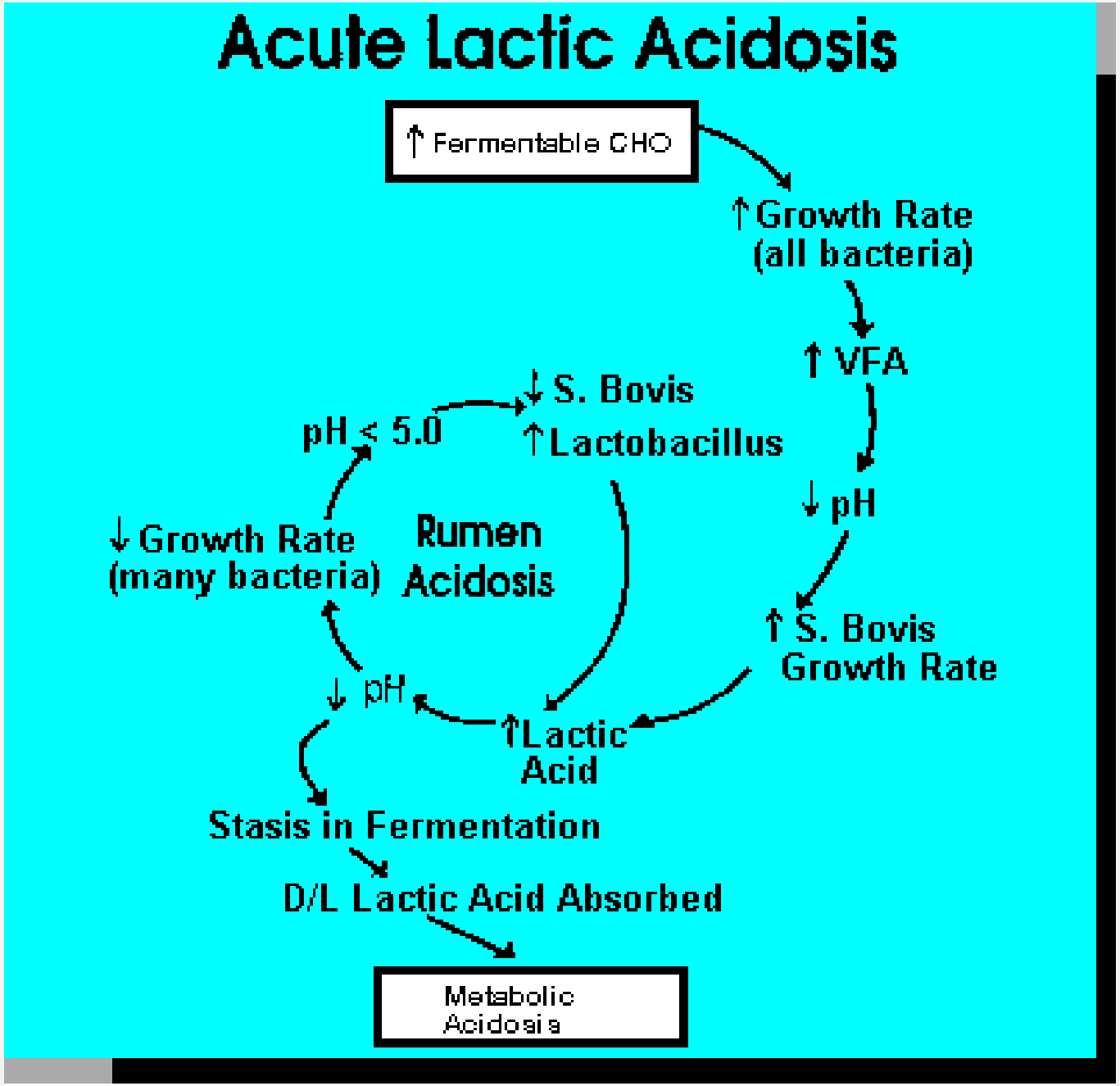


Figure 1. Sequence of events associated with the induction of acute ruminal lactic acidosis (32).

CLINICAL SIGNS

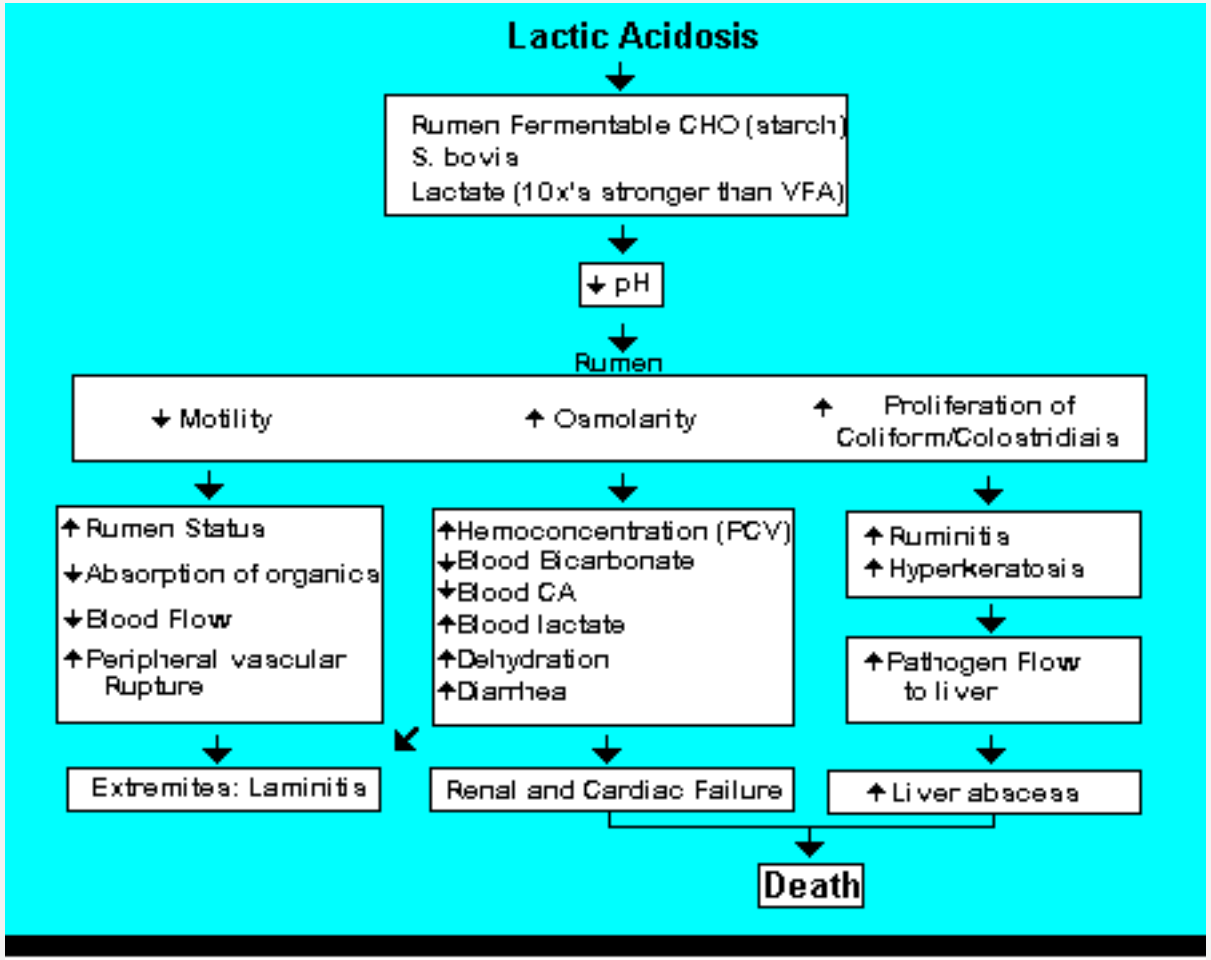
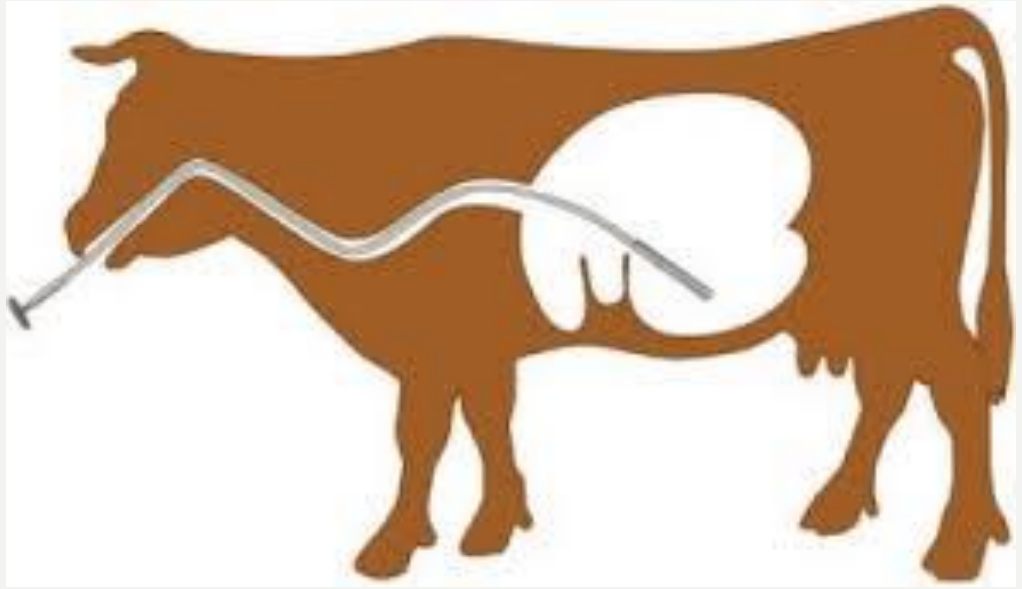


Figure 2. Progression of physiological events taht link acidosis with laminitis (32).

DIAGNOSIS

- A low ruminal pH (<5.5 in cattle unaccustomed to a high grain diet), and examination of the microflora of the rumen for presence of live protozoa. When only one animal is involved and there is no history of engorgement, the diagnosis is less obvious, but the clinical signs



- Increased blood d-lactate and l-lactate and inorganic phosphate concentrations
- Mild hypocalcemia,
- Reduced urinary pH

TREATMENT

- In an animal with a rumen pH of 5.0 or less, a heart rate greater than 100 beats/min, dehydration greater than 8%, and rumen distension and recumbency indicating a severe grain over- load, a rumenotomy should be performed if feasible and the rumen contents evacuated.
- The rumen is then washed with water and emptied several times to remove as much lactic acid as possible.

- The cow is treated with laxatives, fresh hay in the rumen, rumen transfaunates if available, parenteral calcium, and IV fluid therapy
- IV fluids should initially be **hypertonic saline** followed by **balanced electrolyte solutions such as lactated Ringer's solution**, and supplemental **sodium bicarbonate** is added if acidemia is severe (pH <7.15).
- **Flunixin meglumine** should be given to combat excessive prostanoid production and shock.
- **B vitamins** should be administered for several reasons, one of which is that some cattle with ruminal acidosis develop polioencephalomalacia.

- Other treatments may be attempted for animals showing less severe signs and higher rumen pH values or when the number of animals affected precludes rumenotomies.
- One method involves passing a large-diameter stomach tube or Kingman tube and **lavaging the rumen** with warm water several times with the aid of a bilge pump.
- Several flushes with 10 to 20 gallons of water are necessary, and return flow of fluid must be effective for this treatment to be successful.
- After lavage, antacid solutions such as 2 to 4 quarts of milk of magnesia, activated charcoal, and ruminotorics are administered, as well as supportive calcium solutions and IV fluids as indicated.

- Another option that has been used successfully is to simply **drain as much rumen fluid as possible by oral siphon** and **administer 1 to 2 lb of activated charcoal into the rumen.**
- This appears to be effective in **binding rumen toxins** (e.g., endotoxin). Additionally, affected cattle should receive SC administered calcium solutions and IV administered isotonic fluids.
- Cows with moderate to **severe rumenitis** are generally **treated with penicillin** (10,000–20,000 U/kg administered intramuscularly [IM] or SC once daily for 3-5 days) in an effort to prevent bacteremia and liver abscess formation. Broad-spectrum antibiotics should not be used because they may predispose to fungal overgrowth.

SUBACUTE RUMINAL ACIDOSIS

- Subacute ruminal acidosis is caused by ingestion of diets high in rapidly fermentable carbohydrates and/or deficient in physically active fiber.
- Subacute ruminal acidosis is most commonly defined as repeatedly occurring prolonged periods of depression of the ruminal pH to values between 5.6 and 5.2.
- The low ruminal pH is caused by excessive accumulation of volatile fatty acids (VFAs) without persistent lactic acid accumulation and is restored to normal by the animal's own physiologic responses

- Ruminal VFAs are absorbed passively across the rumen wall. This passive absorption is enhanced by finger-like papillae, which project away from the rumen wall and provide massive surface area for absorption.
- Ruminal papillae increase in length when cattle are fed higher-grain diets; this presumably increases ruminal surface area and absorptive capacity, which protects the animal from acid accumulation in the rumen.
- Absorption of VFA inherently increases as ruminal pH drops. These acids are absorbed only in the protonated state. Because they have a pKa of ~4.8, the proportion of these acids that is protonated increases dramatically as ruminal pH decreases below 5.5.

- Ruminal carbohydrate fermentation shifts to lactate production at lower ruminal pH (mostly due to *Streptococcus bovis* proliferating and shifting to lactate instead of VFA production); this can offset gains from VFA absorption.
- Besides disrupting microbial balance, feed deprivation causes cattle to overeat when feed is reintroduced. This creates a double effect in lowering ruminal pH. Cycles of feed deprivation followed by overconsumption greatly increase the risk of subacute ruminal acidosis.

- **Low ruminal pH during subacute ruminal acidosis** also reduces the number of species of bacteria in the rumen, although the metabolic activity of the bacteria that remain is very high. Protozoal populations are particularly limited at lower ruminal pH; the absence of ciliated protozoa in ruminal fluid is often observed during bouts of subacute ruminal acidosis.
- Low ruminal pH may lead to rumenitis, erosion, and ulceration of the ruminal epithelium.
- Once the ruminal epithelium is inflamed, bacteria may colonize the papillae and leak into the portal circulation. These bacteria may cause liver abscesses, which may eventually lead to peritonitis around the site of the abscess.

CLINICAL FINDINGS

- Laminitis may result from release of various mediators, including endotoxins, from rumen microbes destroyed by the pH decreases associated with subclinical rumen acidosis. Mediator absorption is enhanced by chemical damage to the rumen mucosa
- reduced or cyclic feed intake
- decreased milk production
- reduced fat
- poor body condition score despite adequate feed intake,
- unexplained diarrhea

DIAGNOSIS

- Subacute ruminal acidosis is diagnosed on a group rather than individual basis
- Ruminal fluid is collected by rumenocentesis, and its pH is determined on a pH meter.
- Twelve or more animals are typically sampled at ~2–4 hr after a grain feeding (in component-fed herds) or 6–10 hr after the first daily feeding of a total mixed ration.
- If >25% of the animals tested have a ruminal pH <5.5, then the group is considered to be at high risk of subacute ruminal acidosis.

TREATMENT AND PREVENTION

- The key to prevention of subacute ruminal acidosis is allowing for ruminal adaption to high-grain diets, as well as limiting intake of readily fermentable carbohydrates.
- This requires both good diet formulation (proper balance of fiber and nonfiber carbohydrates) and excellent feed bunk management. Animals consuming well-formulated diets remain at high risk of this condition if they tend to eat large meals because of excessive competition for bunk space or after periods of feed deprivation.

- Including long-fiber particles in the diet reduces the risk of subacute ruminal acidosis by encouraging saliva production during chewing and by increasing rumination after feeding.

- Ruminant diets should also be formulated to provide adequate buffering. This can be accomplished by feedstuff selection and/or by addition of dietary buffers such as sodium bicarbonate or potassium carbonate.

- Supplementing the diet with direct-fed microbials that enhance lactate utilization in the rumen may reduce the risk of subacute ruminal acidosis.

- Yeasts, propionobacteria, lactobacilli, and enterococci have been used for this purpose. Ionophore (eg, monensin sodium) supplementation may also reduce the risk by selectively inhibiting ruminal lactate producers and by reducing meal size.