XXX is a 2-week-old Brown Swiss heifer calf that presented to the hospital on April 12, XXXX with calf scours. Upon arrival, she was escorted into a full isolation stall where she could be examined.

HISTORY

As the technician began collecting blood samples for laboratory submission, the student obtained the following history from the owner. XXX had been observed to have diarrhea for the last 4 days, beginning on April 8, XXXX. The consistency of her manure had been watery and yellow, with no evidence of blood. Until then, her diet normally had consisted of 4 pints of milk replacer twice daily. On April 9, April 10 and April 11, the calf received an IV infusion of an electrolyte solution. She had also consumed oral electrolytes on April 10, April 11 and April 12, XXXX. XXX was treated with an unknown dose of florfenecol during this time. At home, the calf had remained weak, but able to stand. She was last offered milk replacer just prior to her arrival at the hospital, but was unable to stand for the feeding. When asked, the owner informed the student that other calves on the farm were also showing signs of diarrhea, but of lessened severity. The calves were all housed in separate hutches.

PATIENT STATUS

Upon presentation to the hospital, XXX was quiet and recumbent, but remained alert and responsive. She had tried to stand, but was too weak. During this unsuccessful attempt, XXX exhibited marked tremors in the forelimbs especially when forced to bear weight.

Physical examination of the calf revealed a rectal temperature of 98.7 F, heart rate of 120 beats per minute, and a respiratory rate of 36 breaths per minute. It is possible that the subnormal rectal temperature (reference range 101.5 F) was due to pneumorectum from the diarrhea, or due to signs of shock. Clinically, the calf appeared to be dehydrated. Her eyes were sunken and her

mucous membranes were tacky but pink with a capillary refill time (CRT) of 2 seconds. She did, however, present with a weak suckle reflex, which is a clinical indicator of relatively normal bicarbonate (HCO3) levels. XXX's cranial nerves, lungs and heart ausculted normally, but her gut sounds were increased, as expected with diarrhea. Her perineum was stained with watery yellow manure, and her weight was estimated at 68 kilograms (kg).

INITIAL DIAGNOSTICS

The blood samples that were collected by the technician for in-house laboratory analysis were submitted for complete blood count (CBC), biochemical profile with electrolytes and a venous blood gas. Manure was also collected at this time and submitted for a *Salmonella* fecal culture. A 14 gauge over the wire IV catheter was placed in the right jugular vein, but IV fluid therapy was not initiated until results of the chemistry profile became available.

Calves may present with diarrhea from a wide array of infectious diseases, usually as a result of failure of passive transfer. Calves presenting with severe diarrhea are often weak, recumbent or comatose as a result of dehydration, hypoglycemia, toxemia or sepsis, electrolyte imbalances, or combinations thereof. A CBC can be a valuable tool to help determine if the calf is suffering from an infectious disease process and whether it is septic. The blood chemistry analysis is used to rule out electrolyte abnormalities that could cause recumbency. It is also vital to the assessment of the liver and kidney function. Because the kidney is the primary organ that compensates for acid- base disturbances within the body, antibiotic and fluid therapy selections will often be determined based on assessment of renal function. While the chemistry panel is also used to provide a general idea of the bicarbonate level using the total carbon dioxide (TCO2) value, the venous blood gas is useful for determining the overall blood pH in addition to the respiratory contribution to the acid-base balance. Finally, the fecal culture for *Salmonella*

species was submitted for two significant reasons. The age of the calf at onset of disease could be consistent with a *Salmonella* infection, and evidence of this pathogen within a dairy herd would have significant implications for the recommendation of management changes. Second, fecal cultures for *Salmonella* are routinely performed on diarrheic animals at the hospital for biosecurity purposes, as these bacteria are highly associated with nosocomial infections in hospitals.

Results of the CBC revealed normal red blood cell (RBC) values, a moderate to large increase in fibrinogen at 900 mg/deciliter (dL) (reference range 200 - 600), and a leukocytosis with a mild left shift. The total white blood cell count (WBC) was 12.84 x 10^3 cells/microliter (uL) (reference range 4 - 12). The elevated segmented neutrophil (SEG) count comprised 70% of the total count at 8.988 x 10^3 cells/uL (reference range 0.6 - 4.0). The number of band cells was increased at 0.257 x 10^3 cells/uL (reference range 0 - 0.12) or 2% of the total, indicating the presence of a left shift. Because both leukocyte migration and fibrin deposition are characteristic of inflammation, we find that this CBC was consistent with an inflammatory leukogram.

Interpretation of the blood gas can be done in a relatively systematic manner, but can become complicated when there is a compensatory response to the primary problem. Three key factors are needed for blood gas analysis: pH, bicarbonate concentration (HCO3) and the rate of alveolar ventilation (pCO2). For the purposes of analysis, it is helpful to understand that HCO3 is an alkaline (basic) buffer, while pCO2 acts as a respiratory acid. Because HCO3 is primarily regulated by metabolic events and kidney function, any disturbances are labeled metabolic in nature. The pCO2 concentration is determined primarily by changes in respiratory function, consequently acid-base disturbances reflected by abnormal pCO2 would be labeled respiratory in

nature. The first step in analysis of the blood gas is done by examining the measured pH. Based on XXX's low pH of 7.271 (reference range 7.31 – 7.53), we can conclude that the calf was mildly acidotic and not alkalotic. The next step is to determine whether there exists a metabolic or a respiratory acidosis by evaluating the HCO3 and pCO2, which can also account for a change in pH. If the HCO3 is decreased and the pCO2 is normal, the disturbance is labeled as a *metabolic* acidosis. If the pCO2 is elevated and the HCO3 is normal, the disturbance is labeled as a *respiratory* alkalosis. XXX's HCO3 was elevated at 35.4 millimoles (mmol) per liter (reference range 17 – 29), as was the pCO2, which measured 76.5 millimeters of Mercury (mmHg) (reference range 35 – 44). From these results we can conclude that XXX had a primary respiratory acidosis with a compensatory metabolic alkalosis.

Results of the biochemical profile were the most remarkable of all testing performed. Because nearly every analyte measured was abnormal, only those of significance to this case will be discussed in detail. Results of all values may be found in appendix 2.

The in-house laboratory at the hospital reports TCO2 and Anion gap (AG) as part of the large animal chemistry profile. Since blood gas and acid-base status have just been discussed, the only remarkable note is that the mild elevation in TCO2 at 31mmol/L (22-29) suggesting that a metabolic alkalosis is present.

One would expect a recumbent calf with diarrhea to have signs of septicemia or toxemia and low blood glucose, as it is readily consumed by circulating bacteria. This, however, was not the case as XXX did not show signs of toxemia based on her CBC, and also presented with a slightly elevated glucose 122 mg/dL (50-79). It is known that steroid hormones produce a gluconeogenic effect, and likely that the stress hormone cortisol produced a similar response in the calf resulting in hyperglycemia.

Phosphorus was the only mineral elevated at 12.1 mg/dL (reference range 4.4 – 9.2). We know that the calf was given a substantial amount of electrolytes both parenterally and orally during the few days prior to admission. Although we do not know the exact content of those electrolytes, it is reasonable to believe that they may have contained some amount of phosphorus. Additionally, it is known that many animals presenting with azotemia will have a concurrent hypophosphatemia. The reduction in glomerular filtration rate (GFR) as is present in animals with azotemia, will lead to reabsorption of phosphorus and a resultant increased serum concentration. XXX's blood urea nitrogen (BUN) and creatinine were both elevated (the definition of azotemia) and will be discussed later in detail.

Creatine kinase (CK) is a "muscle leakage" enzyme that increases with damage to muscle cells or ischemia. The elevated CK value of 2519 units (U)/L (reference range 50 - 271) is a likely result of the calf's recumbency on the day of presentation. Although aspartate aminotransferase (AST) is generally considered a hepatocellular leakage enzyme, it is also present within skeletal muscle and is not organ specific. It is not surprising that the AST was also elevated at 116 U/L (reference range 57 - 108), as it would also be attributed to the recumbency of the calf. It is interesting to note that CK has a relatively short half-life when compared to AST. In the case of chronic disease, this means that CK levels may return to normal while AST levels remain elevated. The fact that both enzymes were elevated in the calf suggests an acute recumbent state, which is supported by the history obtained.

Alkaline phosphatase (AP) and gamma glutamyl transpeptidase (GGT) are generally considered indicators of cholestasis, or impaired bile flow. There are 4 known AP isoenzymes, the most significant of which shows increased activity relative to bone (BAP). The BAP isoenzyme is produced by osteoblasts and increases with activity of those cells. It is reasonable

that a young growing animal like XXX would have an elevated level AP at 504 U/L (reference range 26 - 78) as a result of increases in BAP. When severe enough, cholestasis will result in elevated serum bilirubin levels and while the GGT was elevated at 49 U/L (12-30), the bilirubin remained normal and thus liver disease was not pursued as part of the calf's problem list. GGT is present in high concentrations in the colostrum of all species except the horse, and is a reasonable explanation for elevated serum levels in a two-week-old calf.

The next most significant findings of the chemistry panel were the renal enzymes, which indicated a marked azotemia. The elevated BUN and creatinine were measured at 39 mg/dL (reference range 8 - 22) and 2.2 mg/dL (reference range 0.6 – 1.4), respectively. Azotemia can be classified as pre-renal, renal or post-renal dependent on the cause. It is most likely that XXX presented with pre-renal azotemia, which results from circulatory disturbances such as hypovolemia. A low blood volume would result in decreased renal perfusion, decreased GFR, and increased renal absorption of urea nitrogen into the blood. A response to appropriate fluid therapy will confirm pre-renal azotemia, as correction of hypovolemia should cause BUN and creatinine levels to return to normalcy within 24 to 48 hours. In a case of renal azotemia, GFR decreases as a result of more than 75% of the nephrons becoming non-functional. Fluid therapy will not yield a correction in the serum BUN and creatinine levels. As described earlier, severe pre-renal azotemia can also result in retention of organic acids normally excreted by the kidney and cause other imbalances such as hyperphosphatemia. While BUN and creatinine are both indicators of kidney function, creatinine is not influenced by protein ingestion or catabolism and remains the best indicator of renal function in ruminants.

The electrolytes are the last group to be discussed, and also the most abnormal in severity. Of the three electrolytes discussed, the increase in sodium was the most concerning.

Sodium is the tightly regulated major extracellular cation and its concentration is closely related to extracellular fluid concentration. It is consequently important to take into account the hydration of the patient when making interpretations of sodium measurements. Because sodium levels also determine blood osmolality, a hypernatremic animal will be hyperosmolar as well. XXX had a sodium concentration that measured 193 mmol/L (reference range 140 - 151). The fact that her hydration status was normal (PCV at 42%), makes the sodium value truly significant and not simply a function of concentration due to dehydration. The most likely explanation for the resultant hypernatremia can be based from the history we obtained from the owner. XXX had received both parenteral and oral electrolyte solutions for 3 days. In the absence of enough free water intake, the kidney would have been able to concentrate the urine to a certain point, after which, sodium levels would have remained in the blood after filtration, causing serum concentration levels to rise to a level near incompatible with life.

Potassium is the major intracellular cation and is important for the maintenance of cellular membrane resting potential. Because 60-75% of potassium is found within muscle cells, the total plasma concentration of potassium may not accurately reflect the total body levels. XXX's potassium was markedly elevated, measuring 9.9 mmol/L (3.7-5.6). We discussed earlier the significance of the amount of parenteral and oral electrolytes that this calf received, and it is reasonable to believe that her hyperkalemia was also a result of increased PO intake and IV administration. A second possibility is that, combined with the azotemia and decreased GFR, there would be a decrease in the renal excretion of potassium, causing renal retention and elevated serum potassium levels. A third and final hypothesis for the hyperkalemia can be explained by the process of transcellular shifting. Transcellular shifting occurs when potassium is moved from the intracellular fluid to the extracellular fluid, which assists in preserving normal

pH by decreasing the hydrogen ion concentration in the blood. As the potassium leaves the cell, hydrogen moves into the cell, decreasing the blood pH. While this phenomenon may yield benefits from an acid-base status, the resultant effects of the hyperkalemia can be problematic. As mentioned earlier, potassium is very important for maintaining the resting potential of cells. In the hyperkalemic animal, the cellular resting membrane potential is decreased, exposing the cells to excitability. The most frequent result is the presence of cardiac arrhythmias (which were not observed) but may explain the tremors observed when the calf made an attempt to stand.

XXX also presented with a hyperchloremia as her blood chloride was measured at 148 mmol/L (100-109). Chloride is the major extracellular anion, and found together with sodium. Chloride is necessary for the maintenance of osmolality and acid-base balances. Because changes in free water will alter both chloride and sodium levels proportionally, we are able to calculate a corrected chloride level with the following formula:

Corrected chloride = [normal sodium/measured sodium] x measured chloride

With the values from XXX's chemistry panel, we can determine her corrected chloride:

Corrected chloride = [145/193] x 148 = 111

Based on the corrected value, we can observe that the hyperchloremia is not quite as severe as it first would appear, but is still mildly elevated. One such explanation for this is the fact that HCO3 loss will cause a relative increase in chloride concentration as the body tries to retain the chloride anion in place of the HCO3 anion.

TREATMENT PLAN

A phone call was made to the owner explaining the very guarded prognosis for his calf. Even though the calf was given a mere 10-20% chance of life, the owner gave verbal consent for XXX's treatment to begin. In formulating a plan for treatment, the primary focus was correction

of the hypernatremia. In patients with severe elevations of sodium concentrations, prognosis is very poor because of the cerebral edema that often develops as a result of rapidly decreasing the sodium concentration. Therefore, it is essential that the sodium be decreased in a systematic step-down approach, to allow gradual changes in intracellular concentration. A final isotonic solution containing approximately 140 mEq sodium is the goal. The preliminary plan consisted of the following:

- 0.9% NaCl + 20ml of 7.2% NaCl at 150ml/hr IV (total sodium = 180 mEq) for 6 hours
- 10% Dextrose at 20ml/hr
- Packed Cell Volume and Total Protein (PCV/TP) once daily
- Ceftiofur 5mg/kg (340 mg) IV BID
- Flunixin 0.25 mg/kg (17mg) IV TID
- 2 pints of milk replacer followed by 1 pint plain water QID
- Hourly neurologic evaluation
- Physical exam QID
- Recheck electrolytes after 6 hours of the first hypertonic sodium infusion

The first hypertonic sodium solution was prepared at a slightly lower concentration (180mEq/L) in comparison to the calf's measured sodium (193mmol/L) in order to slowly resolve the hypernatremia for reasons explained above. To correct the hyperkalemia, a 10 % dextrose solution was added. This hyperosmolar solution acts to drive potassium intracellularly. Ceftiofur was added at an increased off-label dose, as recent research has indicated that the spectrum of activity increases with an increase in blood concentration. Ceftiofur is a third generation cephalosporin and at 5mg/kg will provide broad-spectrum coverage against many diarrhea causing bacterial pathogens, specifically Salmonella species. It is also known to have

fewer gastrointestinal side effects, meaning that it does not diminish the normal intestinal flora creating an antibiotic induced diarrhea.

Flunixin is a non-steroidal anti-inflammatory drug (NSAID), which is used at the hospital in 3 different dose regimes. While commonly used for relief of visceral pain, a low dose of 0.25mg/kg given TID is used for 'anti-endotoxic' purposes and was prescribed in the event that the Salmonella cultures were positive. A serious side effect of NSAID use is the formation of ulcers. Flunixin is especially implicated as the cause of abomasal ulcers in ruminants, and prescription of this drug is always carefully considered by veterinarians at the hospital.

The final orders in XXX's treatment plan were related to patient nursing care. Because the calf still had a suckle reflex, feeding orders were established to be administered with a bottle and nipple. The amount of milk replacer offered was based on the amount typically fed on a dairy farm. It was administered in smaller more frequent feedings, as this is generally considered better for patients with gastrointestinal disturbances. Because the calf was on a constant rate infusion of a 10 % dextrose solution, there was little concern that her glucose needs would be met even if the milk replacer was not consumed. The hourly neurologic evaluations were used as a means to identify the presence of cerebral edema. Cranial nerve deficits such as nystagmus, head tilt or pressing or blindness and signs of general CNS deficits such as hyperexcitability, muscle twitching, circling, ataxia and seizures were monitored.

DAILY PROGRESSION

On April 12, XXXX at 1:30 pm, XXX was started on her treatment regime. At 4:00 pm that afternoon, there was no reported change in her condition and she showed no neurologic signs. She made a feeble but unsuccessful attempt to rise as her perineum was cleaned, her nose appeared dry. She was placed in sternal recumbency on the opposite side. At 5:30 pm, a

physical exam was performed and reported unremarkable except for the rectal temperature which remained subnormal at 99.3 F. Her manure was the same watery yellow consistency and she remained free from neurologic deficits. She was able to drink 1 pint of milk replacer with a weak suckle reflex. Blood was obtained for a second chemistry profile and revealed the sodium at 193 mmol/L, potassium at 11.9 mmol/L, chloride at 153 mmol/L, creatinine at 1.7mg/dL and albumin at 2.5 g/dL. These results compared with those taken 5 hours earlier at admission showed a slight worsening of the hypernatremia and hyperkalemia, while the azotemia appeared to be resolving. Because there are after hours fees associated with the in house laboratory performing testing on the weekends, a second sample was taken for a comparison electrolyte analysis performed in the small animal critical care unit on the NOVA blood gas analyzer. The decision was made to continue monitoring the electrolytes with the NOVA system to avoid excess cost to the client. Results from the NOVA were as follows: sodium 197.1 mmol/L, potassium 10.24 mmol/L, chloride 144mmol/L and glucose 111 mg/dL.

At 7:30 that evening, the hypertonic saline solution was stopped and a new hypertonic solution consisting of 0.9% NaCL + 12 ml of 7.2% NaCl (170mEq/L) was added at a rate of 150 ml/hour. The concentration of sodium in this solution was 10 mEq/L less than before. The glucose was increased to 40ml/ hour to further facilitate the intracellular shifting of potassium. Overnight, the calf remained stable on the same course of treatment and was reported to have drunk a small amount of water from a pan. No electrolyte analysis was performed overnight.

Day2

At 8:00 am on April 13, XXXX, a PE revealed a temperature of 99.2 F, heart rate 120 beats per minute and respiratory rate 30 breaths per minute. By 8:30 am, there was reported seizure activity, and 10 mg of diazepam was administered slowly IV for treatment of the seizure.

Electrolyte analysis revealed the following: sodium 178.5 mmol/L, potassium 5.69 mmol/L, chloride 134 mmol/L and glucose 100 mg/dL. It was evident that the electrolytes were slowly returning to normal, and that the seizure activity must be due to the development of cerebral edema. At 10:30 am, a third hypertonic solution of sodium was prepared and administered, consisting of 0.9% NaCl + 8 ml of 7.2% NaCl (165 mEq/L of sodium). Mannitol was also added to the calf's orders at a rate of 0.5 g/kg given as a constant rate infusion over 30 minutes BID. Mannitol is an osmotic diuretic that was prescribed to decrease cerebral edema. Osmotic diuretics are filtered in the glomerulus of the kidney, but are not reabsorbed, allowing plasma concentrations to remain in a hyperosmolar state. As the blood reaches the brain, edema would be reduced as water diffused from the brain tissue to systemic circulation. Administration of the mannitol was challenging, as it crystallizes at high concentrations and lower temperatures. Because the hospital is kept as a temperature controlled environment at 65 F, the mannitol was warmed slightly prior to administration and an in-line filter was placed on the drip set to prevent small crystals from entering XXX's bloodstream.

There was remarkable improvement with the therapy. By 12:00 pm, the calf was able to drink all 2 pints of milk replacer with a much stronger suckle, her nose was moist, and tail was switching, all of which are signs of normal calf behavior. Her PE remained within normal limits except that her manure was changing in color from yellow to greenish yellow with a small amount of frank blood evident. At 6:00 pm, electrolyte analysis revealed sodium 162.4 mmol/L, potassium 5.18 mmol/L, chloride 120 mmol/L and glucose 90 mg/dL. XXX remained bright with a good suckle and was reported to stand without support for the first time. At this time her sodium infusion was again changed to a solution of 0.9% NaCl + 4 ml of 7.2 % NaCl (160mEq/L of sodium).

Day 3

On April 14, XXXX at 4:00 am XXX had another seizure. Diazepam was again administered at 10mg IV slowly. Seizure activity did not cease and a second 10mg dose of diazepam was administered. At 6:00 am the calf was reported as standing, but with muscle fasciculation. At 8:00 am physical examination revealed temperature 105.2 F heart rate 96 beats per minute and respiratory rate 30 breaths per minute. Analysis of her electrolytes revealed sodium 147.1 mmol/L, potassium 4.02 mmol/L, chloride 110mmol/L and glucose 99 mg/dL. She was discontinued from her hypertonic solution and started on a 0.9% NaCl infusion, with 10% dextrose at 30ml/hour. Since all of the electrolytes had returned to normal, the seizure activity had become a primary concern. The following additions were made to her orders:

- Thiamine 680mg in 100ml of 0.9% NaCl
- Potassium penicillin 22,000 IU/kg IV QID (1.5 Million units)
- Dexamethasone 68.5 mg IV once

Thiamine (Vitamin B1) is required for the utilization of glucose in the brain. While the role of thiamine in the neurologic pathway is unknown, some theories suggest that it is involved with nerve impulses as they travel the sodium/potassium gradient. Thus, it is used at the hospital as a neuroprotectant to help preserve normal neurologic function. Dexamethasone is a glucocorticoid often used at the hospital to assist in treatment of neurologic disease. It acts to stabilize cell membranes, but is also known to have a wide range of specific immunosuppressive effects. Because the calf's cause of diarrhea was undetermined, potassium penicillin was added to the order, ensuring broad-spectrum coverage with the ceftiofur, and limiting the onset of secondary infections such as pneumonia. No more seizures were reported on this day, and the calf continued to eat and drink normally. The diarrhea was unchanged.

Day 4

On April 15, XXXX, XXX was normonatremic (140 mmol/L), normokalemic (4.2 mmol/L) and slightly hypochloremic (99 mmol/L). She remained bright with a good suckle and her manure had become semi-formed. Her temperature was slightly elevated at 102.2 but all other PE parameters were within normal limits. She was continued on the treatment plan and did not have any episodes of seizure activity until 8:00 pm that evening. This episode lasted 1-2 minutes and resolved without treatment. It was described as having started with muscle fasciculation in the nose and then a period of circling.

Day 5

On April 16, XXXX, XXX had a few mild seizure episodes lasting only 30 seconds which seem to be initiated by overstimulation. She had received 1 liter of plasma overnight as her total protein seemed to be slowly decreasing likely as a result of a protein losing enteropathy. This is explained by the presence of a compromised intestinal wall (as often occurs with diarrheic patients) resulting in protein loss as it leaks from the intestinal wall into intestinal lumen and is either digested or excreted. The calf remained bright with semi-formed manure and continued to suckle well from the bottle. Her electrolytes had stabilized and in communication with the owner, expectations for long-term improvement were discussed.

Day 6

On April 17, XXXX, XXX continued to show improvement. Her temperature was still mildly elevated at 102.3 F. Seizure activity had decreased to short 10-second bursts of hyperexcitability, and the calf was discontinued from all medications except the flunixin. The resident veterinarian discussed with the owner plans for the calf to go home on Sunday, April 20.

Day 7

On the morning of April 18, XXXX, XXX maintained normal PE parameters, a good appetite, and appeared less hyperexcitable to the student. The flunixin was discontinued and the calf's manure was reported as a soft brown (normal) consistency. She remained on a QID feeding schedule, but by midnight had refused her bottle and was reported as lethargic and weak while standing, although her physical exam was still within normal limits.

Day 8

On April 19, XXXX at 5:45 am, one day prior to discharge, the overnight technician checked on XXX and found her seizing again. The resident was called and a 5 mg dose of xylazine was administered to sedate the calf, as hyperexcitability had historically induced the seizure activity. In the interim of the phone call and arrival of the resident, seizure activity had culminated to an obtunded state. An unreported amount of epinephrine was administered when the resident arrived which produced an audible heartbeat, but no apparent brain activity or responsiveness. The calf died 15 minutes later and was sent to pathology for a necropsy to be performed.

CASE DISCUSSION

Calves may present with diarrhea from a wide array of infectious diseases, usually as a result of failure of passive transfer. Calves are born with a naive immune system and failure of passive transfer occurs when there is insufficient absorption of immunoglobulins (IgG) from colostrum, resulting in a compromised disease defense mechanism. Current recommendations for a modern day Holstein heifer calf are to ensure 1 gallon of high quality colostrum (yielding ideally 200grams of IgG) within the first 6 hours of life. A relatively inexpensive means by which IgG absorption is assessed at the hospital is by measuring the total protein. Calves must be less than 1 week old but should have received the last colostrum feeding at least 6 hours prior

to testing. A total protein concentration measured at $\geq$ 5.5 g/dL has been proven to clinically correlate with an IgG concentration of $\geq$ 1200mg/dL, which is the goal for adequate protection in the individual calf.

Many pathogens are known to cause diarrhea in calves 3 weeks of age or younger. The most common of these include *E.coli, Salmonella*, Rota and Corona Viruses, Clostridium and Cryptosporidium. Treatment of the diarrheic calf will include PO or IV of fluids usually containing sources of electrolytes and dextrose. Antibiotic therapy is often used in conjunction with fluid therapy, but ideally should be reserved for calves showing signs of systemic illness.

Hypernatremia, commonly known as salt toxicity occurs when sodium intake increases in the absence of free water intake. Sodium ions from the blood accumulate in the CSF by diffusion, resulting in a hyperosmolar state. Cerebral edema results when there is a rapid change to normal plasma osmolality. When normosmolar blood reaches the hyperosmolar CSF and neurons, water diffuses from the blood into these tissues, resulting in edema, intracranial pressure and acute encephalopathy.

Recommendations for treatment of cerebral edema include the administration mannitol at a rate of 0.25-2 g/kg twice daily. Dexamethasone is recommended at 1-4mg/kg IV or BID. Dimethyl Sulfoxide is often used as an anti-inflammatory for the treatment neurologic disease, but its use is strictly prohibited in cattle and was therefore not a treatment option. XXX had received a 0.5 g/kg dose of mannitol and a 1 mg/kg dose of dexamethasone, both appropriate prescriptions based on current recommendations. Normonatremia was achieved over the course of 4 days treatment with IV treatment 4 different hypertonic saline solutions. Additional therapeutics including neuroprotectants, glucocorticoids, NSAIDS and antibiotics were used, and nursing care was provided at the highest level possible.

It was unfortunate that XXX died only 1 day prior to discharge, but her owner allowed a necropsy to be performed so that a cause of death could be determined. The most significant finding observed from the gross necropsy revealed a perforating abomasal ulcer with extensive fibrous peritonitis. The umbilical area was devoid of inflammation, suggesting that the original source of infection was not via the umbilicus. The histological analysis supported the gross findings reporting a severe mutifocal ulcerative gastritis and an acute to subacute fibrionsupperative peritonitis. Other findings included fibrinous cholecystits and serositis, lymphoplasmacytic supperative myocarditis, and supperative bronchopneumonia. The pathologist commented, "… acute CNS clinical signs do not correlate well with histopathological findings. No significant findings were present in the brain and cerebral edema could not be confirmed."

Abomasal ulcers affect ruminants of all ages and occur as perforating and non-perforating types. Fever and peritonitis may or may not be present, depending on the severity of mucosal damage. Perforating ulcers with peritonitis are common in milk fed calves, but the exact etiology is not known. It is believed that a combination of factors such as feeding frequency, environmental stress, mechanical abrasion from ingestion of roughages, mineral deficiencies and infection with *Clostridium perfringens* type A or certain types of fungi may contribute to the formation of ulcerative lesions.

Flunixin, as mentioned earlier, is a NSAID, which is a very potent inhibitor of cyclooxygenase (COX). COX is an enzyme that is responsible for the formation of prostanoids, including the many types of prostaglandins. Target specific prostaglandins have many functions within the animal, including decreasing gastric acid secretion and increasing gastric mucous secretion. When COX is inhibited, prostaglandin E2 synthesis decreases resulting in increased

gastric acid secretion and decreased mucous secretion. Abomasal ulcers form readily under these conditions. While higher doses of flunixin can be associated with ulcer formation, the low dose that XXX received (0.25mg/kg IV TID) was unlikely associated with the perforating ulcer seen on necropsy, as this dose does not yield anti-inflammatory properties and has no effect on prostaglandin. More likely, the stress associated with diarrhea and hypernatremia were factors that ultimately caused the demise of this calf.

Appendix 1 : Complete Blood Count

DATE	TEST	RESULT	UNITS	REFERENCE RANGE
4/12/XX	Specimen Appearance	Normal		-
Admission	Plasma Appearance	Normal		-
	Total Plasma Protein	6.5	g/dL	6-8
	Fibrinogen	900 H	mg/dL	200-600
	RBC	9.8	X 10^6/ uL	5-10
	Hemoglobin	14.7	g/dL	8-15
	RBC Hemoglobin	13.6	g/dL	8-15
	Hematocrit	43	%	24-46
	Packed Cell Volume	42	%	24-46
	MCV	43.5	fL	40-60
	MCH	15.0	Pg	11-17
	MCHC	34.4	g/dL	30-36
	RDW	21.4	%	-
	Platelet	400	X 10^3/uL	200-800
	MPV	6.0	fL	-
	Platelet Estimate	Appears WRI		-
	Anisocytosis	1+		
	Poikilocytosis	2+		
	Acanthocytosis	2+		
	Crenation	3+		
	WBC	12.84 H	X 10^3/uL	
	SEG	8.988 H (70%)	X 10^3/uL	
	BANDS	0.257 H (2%)	X 10^3/uL	0-0.12
	LYMPH	2.825 (22%)	X 10^3/uL	
	MONO	0.770 (6%)	X 10^3/uL	
	Döhle Bodies			
	Atypical Lymphs			
	Comments			

Appendix 2 : Plasma Biochemical Profile

DATE	TEST	RESULT	UNITS	REFERENCE RANGE
4/12/XX	Sodium	193.0 H	mmol/L	140-151
Admission	Potassium	9.9 H	mmol/L	3.7-5.6
	Chloride	148 H	mmol/L	100-109
	TCO2	31 H	mmol/L	22-29
	Anion Gap	24		-
	Calcium	9.9	mg/dL	7.9-10.5
	Phosphorus	12.1 H	mg/dL	4.4-9.2
	Magnesium	2.9	mg/dL	1.8-2.9
	Glucose	122 H	mg/dL	50-79
	Urea Nitrogen	39 H	mg/dL	8-22
	Creatinine	2.2 H	mg/dL	0.6-1.4
	Total Protein	5.7 L	g/dL	6.3-8.5
	Albumin	2.6 L	g/dL	3.2-4.3
	Globulin	3.1	g/dL	-
	Alkaline Phosphatase	504 H	U/L	26-78
	Creatine Kinase	2519 H	U/L	50-271
	AST	116 H	U/L	57-108
	Gamma GT	49 H	U/L	12-30
	Cholesterol	61 L	mg/dL	112-331
	Total Bilirubin	0.2	mg/dL	0.1-0.4

Appendix 3 : Venous Blood Gas

DATE	TEST	RESULT-MEASURED	RESULT-CORRECTED	UNITS	REFERENCE RANGE
4/12/XX	pH	7.271	7.270		
Admission	pCO2	76.3	76.5	mmHg	
	pO2	42.5	42.7	mmHg	
	SO2 %	65.3		%	
	Hct	24		%	
	Hb	7.7		g/dL	
	BEecf		8.3	mmol/L	
	BEb		8.1	mmol/L	
	SBC		31.4	mmol/L	
	HCO3		35.4	mmol/L	
	TCO2		37.8	mmol/L	
	A		50.5	mmHg	
	P50		28.6	mmHg	
	O2Cap		10.6	mL/dL	
	O2Ct		7.1	mg/dL	

Appendix 4 : Electrolyte Analysis

DATE	4/12/XX	4/12/XX	4/13/XX	4/13/XX	4/14/XX	4/15/XX	4/16/XX	4/17/XX	REF RANGE
TIME	5:30 p	4:58p	8:36a	5:10p	8:23a	8:26a	7:23a	8:21a	
Sodium (mmol/L)	194.0 H	197.1	178.5	162.4	147.1	140.0	130.6	129.4	140-151
Potassium (mmol/L)	11.9 H	10.24	5.69	5.18	4.02	4.2	4.45	4.37	3.7-5.6
Chloride (mmol/L)	153 H	144	134	120	110	99	93	85	100-109
Glucose (mg/dL)		111	100	90	99		109		
TCO2 (mmol/L)	29					27			22-29
Anion Gap	24					18			
Creatinine (mg/dL)	1.7 H								0.6-1.4
Albumin (g/dL)	2.5 L								3.2-4.3

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