Cow/Calf Session I

Moderator: **Mark F. Spire**

Neonatal Physiology and Fluid Therapy of Calves

Allen J. Roussel, Jr., *DVM, MS*
Diplomate ACVIM
The Texas Veterinary Medical Center
College of Veterinary Medicine
Department of Large Animal Medicine & Surgery
College Station, Texas 77843-4475

Part 1: Neonatal Physiology

The maturation of an animal from embryo to "old age" is a continuum characterized by periods of rapid change and periods of relative stability. As the animal completes the change from existence *in utero* to life as an independent entity, many changes occur quickly. The degree of maturity of neonates of different species varies as does the maturity of organ systems within a species. Other papers in the proceedings will address neonatal physiology as it relates to pharmacology and immunology while this paper will focus on changes in blood and plasma constituents, and fluid and electrolyte homeostasis.

Hematology and Clinical Chemistries

Tennant *et al* described in detail the changes in blood cell parameters that occur in dairy calves during the neonatal period. Relative red cell mass as measured by packed cell volume falls consistently during the first week, especially the first 24 hours. During the early neonatal period, there is extreme variability in hematocrit of clinically normal calves (20%-50%). White blood cell (WBC) counts and relative proportions of white cell types undergo significant change during the first week of life. Term calves born by vaginal delivery typically have a neutrophilic, lymphopenic leukocytosis when compared to mature cattle. This is thought to be the result of glucocorticoid release by the fetal adrenal gland, which is part of the hormonal signaling for the initiation of parturition. Total WBC count drops significantly for 48 hours. The neutrophil count decreases and the lymphocyte count increases until, by Day 5, the relative proportions of neutrophils to lymphocytes approximates that of mature cattle.

A complete, concise study on clinical chemistry values of neonates is not readily available, but even if it was, it would be much less useful than that of hematologic values because reference ranges for clinical chemistries tend to be different for each laboratory. Therefore, it is more useful to be aware of relative differences between neonatal and mature cattle rather than absolute values. Total protein concentration of calves is usually lower than that of mature cattle. Albumin is consistently slightly lower, while globulins are almost totally dependent upon colostral transfer and can vary greatly in clinically healthy calves. Another serum constituent appearing on many chemistry profiles that varies with colostral intake is gamma glutamyl transferase (GGT). Boyd demonstrated that GGT rises about 62-fold following ingestion of colostrum. It has been suggested by some that GGT is a useful indicator of passive transfer. Other enzymes that rise slightly after ingestion of colostrum (or pasteurized milk) by neonates include lactate dehydrogenase, alkaline phosphatase, creatine kinase and aspartate transferase. Resting serum glucose concentration is considerably higher during the neonatal period than during maturity.

The Gastrointestinal Tract

The gastrointestinal tract of the preruminant calf differs in several ways from that of the mature cow. The relative sizes of the functional compartments of the stomach change dramatically as the calf matures. At one day of age, the rumino-reticulum represents only 34% of the stomach while the abomasum comprises 56%. For suckling calves on pasture, by Day 28 that ratio is almost exactly reversed, the rumino-reticulum accounting for 55% and the abomasum, 34%. At maturity the rumino-reticulum, omasum and abomasum comprise 64%, 25%, and 11% of the stomach, respectively.

As the calf's diet changes from milk to roughage, the pH of the rumino-reticulum increases. As the pH of the rumino-reticulum becomes compatible with protozoal life, faunation of the organ occurs. Ruminal bacteria and pro-

tozoa are transferred from mature ruminants by licking and grooming, or eating from common sources. In calves on pasture, protozoal faunation takes place between 30 and 60 days of age.

The ability of cattle to digest and absorb carbohydrates changes rapidly in early neonatal life. Oral lactose and glucose tolerance tests conducted at 3 to 4 days, and again 5 days later, show significant flattening of the plasma glucose curves in the older calves. It was not proven whether changes in absorption or hepatic metabolism were responsible, but in a separate study mucosal lactase was shown to decrease dramatically in the first 3 weeks of a calf's life. Sucrase is absent from the calf's intestinal tract; therefore, sucrose (table sugar) cannot be digested. In fact, it causes severe osmotic diarrhea if administered in sufficient quantity.

The Kidney

The kidney of the calf is most mature, relative to the adult, of the domestic species. The concentrating ability of the calf is approximately one-half that of the mature cow, and twice that of the neonatal human being, dog or rat. Renal retention and excretion of electrolytes is also relatively efficient. If the calf's kidneys were not able to conserve water and electrolytes, imagine how devastating neonatal diarrhea would be to the species.

Part II - Fluid Therapy

The leading cause of dehydration and electrolyte imbalance in neonatal calves is diarrhea. Although there are many infectious agents that cause diarrhea in calves, the net effect on fluid and electrolyte balance is relatively consistent and predictable. The important abnormalities which frequently exist and should always be addressed when treating dehydrated calves are:

1) Fluid and electrolyte depletion
2) Acidosis
3) Net energy deficit and/or hypoglycemia

Fluid and Electrolyte Depletion

Diarrhea, which is frequently accompanied by decreased intake, can rapidly cause serious total body fluid depletion of neonatal calves. Total body deficits of 12% or greater can occur, the loss being first and greatest from the intravascular compartment followed by the interstitial compartment and intercellular compartment, respectively.

The total amount of fluid to be administered should be calculated for the first day by estimating the deficit (percent dehydration x body weight in kg) and adding maintenance (50 ml/kg) and anticipated loss (2 liters for moderate to severe diarrhea). If the estimated degree of dehydration is greater than 8%, or the calf is recumbent or refuses to suckle, intravenous replacement therapy is indicated. A formulation that has been successful in our hands appears in Table 1. At least 2 liters, but preferably 4 liters, should be administered intravenously. The balance of the requirements can be given by the oral route. The rate of intravenous administration is important to bovine practitioners because restraint facilities and technical assistance are often lacking in practice. Kasari and Naylor suggested that 70 ml/kg/hr was a maximum safe rate for an isotonic balanced rehydration solution. That's about 3 liters per hour to a 100 pound calf. Sodium (Na), the major extracellular cation, is usually lost in relatively equal or greater proportion to water by diarrheic calves. Hence, when serum Na from a dehydrated calf is measured, it is usually within normal limits or slightly decreased. Therefore, replacement fluids should contain Na in concentrations approximately equal to that of plasma. Otherwise, the dilutional effect on plasma Na will result in renal exertion of free water, which will diminish the effectiveness of fluid replacement therapy. Potassium (K) depletion also occurs during diarrhea, but it usually cannot be detected by conventional laboratory evaluation. In fact, K is often increased in the plasma of dehydrated calves despite the fact that K is lost in the feces and urine. This increased plasma K, occurring simultaneously with total body K deficit, is a result of acidosis. In response to acidosis, K shifts from the intracellular fluid, where about 95% is normally found, into the intracellular fluid. Therefore, plasma K is elevated but total body K is decreased. When the blood pH returns to normal, K moves back into the cells and plasma K goes down, often to sub-normal concentrations. Therefore, K replacement therapy should accompany alkalinization. Oral replacement is safest, but administering up to 20 mEq/L K intravenously along with glucose and sodium bicarbonate is safe and this combination usually results in a *decrease* in plasma K.

Table 1. A formula for rehydration of calves by intravenous infusion.

NaCl	10 g
KCl	4 g
$NaHCO_3$	20 g
Dextrose	50 g
Water	1 gallon

Acidosis

Acidosis results from loss of Na and K, unaccompanied by loss of a strong anion according to the strong ion theory of acid-base balance. Traditional theory explained acidosis by a loss of bicarbonate. In addition to electrolyte loss, there is a concurrent accumulation of lactic acid as peripheral perfusion decreases and tissue hypoxia occurs. If acidosis is moderate to severe ($pH \leq 7.25$), it must be corrected by specific therapy, not simply volume replacement. Kasari and Naylor, and Boothe and Naylor showed that intravenous and oral replacement therapy without alkalinizing agents did not correct acidosis of diarrheic calves. Acidosis is corrected by replacing Na unaccompa-

nied by a strong anion. This is usually accomplished by administering solutions containing sodium salts of bicarbonate, lactate, acetate, or citrate. Intravenous sodium bicarbonate administration resulted in the most effective alkalinization of acidotic calves, followed by lactate and acetate, which were equivalent. Naylor found that sodium gluconate administered intravenously to calves did not result in alkalinization. Sodium citrate is an acceptable alkalinizing agent when administered orally, but its calcium-chelating properties make it unacceptable as an agent for intravenous administration.

In studies performed using calves, there appeared to be no strong advantage of acetate or lactate over the other. While it has been shown that lactate is metabolized more slowly by calves with lactic acidosis, the studies of Kasari and Naylor cast doubt on the clinical significance of this fact. One thing that should be considered when comparing solutions, however, is that lactate exists in a D- and L-isomeric form while acetate does not. Commercial lactated ringers solution contains 50% D-lactate and 50% L-lactate, but only the L isomer is metabolized efficiently by mammals. Therefore, the alkalinizing potential of racemic lactate is less than that of acetate if administered in equimolar quantities.

If blood gases or total CO_2 measurement is available, the following equation can be used to estimate the total body requirement of base (or, more correctly perhaps, strong cation):

$$\text{Total Deficit} = \text{Base Deficit} \times 0.6 \times \text{Body Weight (kg)}$$

If measurement of base deficit is not possible, one may make an estimate based on Naylor's work. When estimating the base deficit, a reasonable guess if the calves are moderately to severely dehydrated and depressed is 12 mEq/L for calves a week or younger and 20 mEq/L for calves over a week of age. That means a 40 kg calf needs about 288 mEq (or 12 g) $NaHCO_3$ if a week of age or younger and 480 mEq (or 40 g) if older than one week. While it is certain that alkalinizing agents are needed to correct acidosis, it is also important to mention that over-alkalinization is possible. If the total base deficit is replaced by intravenous infusion and alkalinizing oral rehydration solution (ORS) is given for the next several days, there is reasonable chance of causing alkalosis.

This brings us to the matter of alkaline and alkalinizing ORS - not the same thing. Bicarbonate-containing solutions are *alkaline* and *alkalinizing,* but solutions containing acetate or citrate are *acidic* and *alkalinizing.* Several years ago it was shown that mixing milk replacer and ORS 1:1 causes diarrhea, and it was suggested that those solutions containing bicarbonate were more likely to produce the problem because of inhibition of the rennet clot in the abomasum. Therefore, it became common practice to feed milk replacer or milk and ORS separately, several hours apart. Recent work by Heath *et al* suggests that even when ORS is not given mixed with milk, bicarbonate-containing solutions may decrease weight gains in diarrheic calves fed milk and ORS on the same day. They suggest feeding diarrheic calves their normal milk ration plus non-bicarbonate-containing ORS; that is, non-bicarbonate-containing ORS with *alkalinizing* potential. Some ORS does not have significant alkalinizing potential and should only be used for calves with mild diarrhea or after acidosis has been corrected.

Net Energy Deficit and/or Hypoglycemia

Clinical hypoglycemia is not common in diarrheic calves, but it can be severe. My recommendation is to include glucose at 1-2% in all rehydration solutions for intravenous administration to calves (Table 1). To my knowledge, all commercially available brands of ORS contain enough glucose to correct hypoglycemia, but they vary greatly in their total energy content. In an attempt to supply calves with adequate energy during fasting, manufacturers of ORS have added more and more glucose to their products, creating significantly hyperosmotic solutions. The need for all this glucose might be questioned now that fasting is losing favor with many veterinarians. Fasting will reduce fecal output in malabsorptive diarrheas, probably the most common type seen in calves; however, fasting also results in greater weight loss or less weight gain, and loss of mucosal enzymatic activity. Feeding during rehydration is becoming very popular in human medicine as well as in veterinary medicine. Therefore, very high glucose solutions may have limited usefulness.

The question of hyperosmolality has been debated for years without a clear consensus being reached. Hyperosmolar solutions have been used successfully for years. Recently, Levy *et al* published a study and showed no difference between the ileal effluent of calves receiving hyperosmolar OSR compared to those receiving isomolar ORS. That is, the small intestine of the normal calf was able to absorb the extra glucose load with no excess glucose being passed to the colon. Whether the same results would be obtained in calves with viral enteritis is debatable. My personal opinion is that high-energy solutions should be reserved for situations: 1) where fasting is practiced, and 2) when ambient temperature is extremely low. Milk-feeding should be encouraged, especially multiple small feedings, which mimick the calf's natural feeding behavior. Moderately hyperosmotic ORS (400-550 mosmols) probably contain adequate supplemental energy if the calf is also consuming milk at 8-10% body weight.

In summary, fluid and electrolyte therapy of calves should not be a complicated or technically difficult procedure. A few simple rules can be followed to optimize the value of this life-saving treatment. Using the principles discussed above, each practitioner should be able to formulate a standard protocol for fluid therapy that requires few modifications and provides high quality professional service to the client and his livestock.