Effect of continuous intravenous administration of a 50% dextrose solution on phosphorus homeostasis in dairy cows

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Objective—To determine the effect of continuous IV administration of 50% dextrose solution on phosphorus homeostasis in lactating dairy cows.

Design—Clinical trial.

Animals—4 multiparous Jersey cows.

Procedures—Cows were administered 50% dextrose solution IV (0.3 g/kg/h [0.14 g/lb/h]) for 5 days. Plasma concentrations of glucose, immune-reactive insulin (IRI), and phosphorus were determined before, during, and for 72 hours after dextrose infusion. Phosphorus intake and losses of phosphorus in urine, feces, and milk were determined. Each cow received a sham treatment that included instrumentation and sampling but not administration of dextrose.

Results—Plasma glucose, IRI, and phosphorus concentrations were stable during sham treatment. Plasma phosphorus concentration decreased rapidly after onset of dextrose infusion, reaching a nadir in 24 hours and remaining less than baseline value for 36 hours. Plasma phosphorus concentration increased after dextrose infusion was stopped, peaking in 6 hours. Urinary phosphorus excretion did not change during dextrose infusion, but phosphorus intake decreased because of reduced feed intake, followed by decreased fecal phosphorus loss and milk yield. Rapid changes in plasma phosphorus concentration at the start and end of dextrose infusion were temporally associated with changes in plasma glucose and IRI concentrations and most likely caused by compartmental shifts of phosphorus.

Conclusions and Clinical Relevance—Hypophosphatemia developed in response to hyperglycemia or hyperinsulinemia in dairy cows administered dextrose via continuous IV infusion. Veterinarians should monitor plasma phosphorus concentration when administering dextrose in this manner, particularly in cows with decreased appetite or preexisting hypophosphatemia. (J Am Vet Med Assoc 2006;229:413–420)

Fifty percent dextrose solution is frequently administered IV to periparturient dairy cows as a treatment for ketosis or hepatic lipidosis.12 Intravenous administration of dextrose is also empirically used as a supportive treatment in cows that are inappetent or recumbent or have gastrointestinal or infectious diseases. Cows with hepatic lipidosis or prolonged anorexia sometimes require continuous IV infusion of dextrose for several days until they can maintain energy balance.3 Continuous IV infusion of dextrose or other carbohydrate solutions can result in severe hypophosphatemia in humans and other monogastric animals.5,6 To our knowledge, the effect of continuous IV infusion of 50% dextrose solution on plasma P concentration in dairy cows has not been reported.

Urine is the main route of P excretion in monogastric animals, whereas saliva is the main route of P excretion in dairy cows.8 Dairy cows can also lose a substantial amount of P in milk. Sudden loss of P in milk at the onset of lactation and reduced dietary P intake accompanying ketosis, hepatic lipidosis, and other periparturient diseases predispose periparturient cows to hypophosphatemia.7 A further reduction in plasma P concentration as a result of dextrose administration might adversely affect a cow’s recovery or even result in recumbency.13 The purpose of the study reported here was to determine the effect of continuous IV administration of 50% dextrose solution on plasma P concentration in lactating dairy cows and investigate potential homeostatic alterations responsible for dextrose-associated hypophosphatemia. We hypothesized that an aggressive rate of dextrose administration (0.3 g/kg/h [0.14 g/lb/h]) would result in hypophosphatemia. Results of the study were expected to be relevant to veterinarians who treat dairy cows, particularly those at teaching hospitals or haul-in practices where continuous IV infusion of dextrose is most likely to be performed.

Materials and Methods

Four multiparous Jersey cows from the University of Illinois dairy herd from 80 to 120 days in lactation were assigned to a duplicated 2 × 2 Latin square study design. Cows were judged as healthy on the basis of results of physical, serum biochemical, and hematologic examinations. Milk production at the start of the study ranged from 26 to 36 kg/d. Each cow received an experimental treatment of 50% dextrose solution IV for 5 days at a rate of 0.3 g/kg/h and a sham treatment that consisted of identical instrumentation.
without dextrose administration. Two cows received the experimental treatment first and 2 received the sham treatment first, as determined by flipping a coin. A washout period of at least 3 days was maintained between treatments to allow cows to return to pretreatment feed intake and milk production. At the conclusion of the main study, 2 of the cows were assigned to a feed-matched control treatment, in which they were instrumented and fed the amount of feed consumed during the experimental treatment but were not given dextrose. All methods were approved by the University of Illinois Institutional Animal Care and Use Committee.

Cows were housed on unbedded rubber mats in individual tie stalls in a temperature-controlled building. Physical examinations were performed daily. Cows were fed a TMR based on corn silage, ground corn, haylage, wet brewers grains, cotton seed, hay, and soybean meal. The ration was formulated to meet the nutrient requirements of lactating dairy cows according to recommendations of the National Research Council with 17.5% crude protein, 22% acid detergent fiber, 35% neutral detergent fiber, 0.87% Ca, 0.29% P, 0.89% Na, 0.48% K. The TMR was delivered with 1.2% of feed as Mcal of energy for lactation/kg of DM. Feeding times were 8:30 am and 8:30 pm. Remaining feed was removed 1 hour before each meal to allow a 60-minute nonfeeding period before saliva sampling. Cows were milked twice daily at 7 am and 7 pm.

After 7 days of acclimatization, each of the 4 cows was asexually fitted with 2 indwelling extension-usable jugular catheters. A 16-g, 83-mm catheter was placed approximately 10 cm below the mandible, and an extension set was attached for blood collection. A 14-g, 133-mm catheter was placed approximately 15 cm below the 16-g catheter, and an extension set was attached for IV dextrose administration. Both extension sets were sealed with injection caps, and catheters were sutured to the skin.

The amount of 50% dextrose solution required in 13 hours was transferred aseptically into a sterile carboy. A 16-g, 83-mm catheter was placed approximately 10 cm below the mandible, and an extension set was attached for blood collection. A 14-g, 133-mm catheter was placed approximately 15 cm below the 16-g catheter, and an extension set was attached for IV dextrose administration. Both extension sets were sealed with injection caps, and catheters were sutured to the skin.

Blood was collected from the sampling catheter 24 and 12 hours before the start of each treatment period. Within each treatment period, blood was collected immediately before beginning the dextrose or sham infusion at 8 am and 5, 10, 20, 40, 90, 180, 360, and 720 minutes later. Blood was then sampled at 12-hour intervals at 8 am and 8 pm, shortly before the morning and evening meals. At the end of the infusion phase, blood was collected immediately before discontinuing the dextrose or sham infusion and 5, 10, 20, 40, 90, 180, 360, and 720 minutes later. Thereafter, blood was again sampled at 12-hour intervals until 72 hours after the end of the infusion phase.

The sampling catheter was flushed with 3 mL of heparinized saline (0.9% NaCl with 10 U of sodium heparin/mL) before 5 mL of blood was withdrawn and discarded. Blood was then collected by syringe and transferred to appropriate tubes. The catheter and extension set were flushed with 10 mL of heparinized saline solution after sampling. If sampling times were more than 10 minutes apart, the catheter and extension set were filled with sodium heparin (1,000 U/mL) to ensure patency; the heparin was withdrawn and discarded at the next sampling time.

Blood for plasma biochemical analysis was dispensed into prechilled evacuated tubes containing sodium heparin. Tubes were immediately placed on ice and centrifuged within 1 hour. Harvested plasma was stored at 4°C for up to 12 hours. Concentrations of P, Ca, albumin, creatinine, and glucose were determined spectrophotometrically, and concentrations of Na, K, and Cl were determined by ion-selective electrodes. Plasma osmolarity was measured by freezing-point depression within 2 hours after sample collection. An aliquot of plasma was frozen at -80°C until assayed for IRI by use of a radioimmunoassay validated for cattle.

Hematologic and blood gas analyses were performed on blood samples collected every 12 hours. Blood for hematologic analysis was dispensed into evacuated tubes containing EDTA. Erythrocyte concentration, Hct, hemoglobin concentration, mean corpuscular volume, and mean corpuscular hemoglobin concentration were determined by use of an automated hematologic analyzer. Blood smears were examined for abnormal erythrocyte morphology by an investigator (AMB) who was unaware of treatment group assignments. To determine blood gas tensions and pH, blood was collected anaerobically into prechilled, heparinized 2-mL syringes. Samples were placed on ice and analyzed within 1 hour.

The amounts of TMR fed and refused were recorded. A 100-g sample of fresh TMR was collected daily and composited into 300-g samples every 3 days. Dry matter was determined by air drying to 100°C to constant weight. Dried samples were stored in air-tight plastic bags at 21°C until P concentration was determined by use of inductively coupled plasma spectrophotometry. Daily DMI was calculated from feed intake. DM, and P concentration values. Remaining feed was not analyzed for P concentration because of probable saliva contamination.

The method described by Fellner et al. was used to collect urine. Briefly, a conforming cup was secured over the cow's vulva with self-adhesive tape, and urine was collected into a clean plastic jar attached via tubing. Urine volume was measured at 12-hour intervals when the jars were emptied (at 7:30 am and 7:30 pm). After thorough mixing, samples were obtained and stored at 4°C for up to 12 hours until they were analyzed for osmolality, P, Ca, creatinine, Na, K, Cl, and glucose concentrations as described for plasma. Renal excretion values for biochemical analytes were calculated for each 12-hour collection period by multiplying the concentration of the analyte by the volume of urine collected in 12 hours. Daily P concentration values were calculated from feed intake. DM, and P concentration values. Remaining feed was not analyzed for P concentration because of probable saliva contamination.

Milk yield was recorded and samples were collected from the bucket of the milking machine at each milking.
Samples were frozen at –20°C until they were analyzed for P. Milk P loss was calculated from milk P concentration and kilograms of milk produced.

All feces were collected into individual pans located beneath the stalls. Pans were cleaned daily at 9 am. Feces were weighed and thoroughly mixed, and samples were stored at –20°C until they were analyzed for DM and P. Before analysis, samples were homogenized in a blender for 40 seconds. Dry matter was determined via atmospheric oven drying at 100°C to constant weight. Fecal P concentration was determined by use of a dry-ash digestion procedure via inductively coupled plasma spectrometry. Daily fecal P loss was calculated by multiplying fecal P concentration by kilograms of fecal DM.

Statistical analysis—Results are expressed as mean ± SD or as geometric mean and range. A statistical software package was used for analysis. Values were log transformed or ranked when necessary to achieve a normal distribution. Repeated-measures ANOVA was used to detect differences in measured variables between treatment groups and over time. Bonferroni-adjusted P values were used to assess differences within and between treatment groups whenever the F test was significant. Values of P < 0.05 were considered significant.

Results

No changes in plasma glucose concentration (overall mean, 65 ± 5 mg/dL), IRI concentration (overall mean, 6.7 ± 1.2 µU/mL), or P concentration (overall mean, 3.7 ± 0.7 mg/dL) occurred in sham-infused cows (Figure 1).

Plasma glucose concentration began to increase immediately after the start of IV dextrose infusion (Figure 1) and was higher in dextrose-treated cows than sham-treated cows from 5 minutes until the infusion was discontinued. Plasma glucose concentration peaked at 6 hours before decreasing to a mean value of approximately 100 mg/dL during the next 6 hours. Mean plasma glucose concentration remained fairly constant thereafter until 96 hours, although there was substantial intercow variability. At 96 hours, mean plasma glucose concentration decreased to approximately 80 mg/dL, where it remained for the duration of the infusion phase. After

Figure 1—Mean ± SD plasma glucose, IRI, and P concentrations in 4 lactating Jersey cows administered 50% dextrose IV (0.3 g/kg/h [0.14 g/lb/h]) for 5 days (dashed lines) and in the same cows (controls) during sham infusion (dotted lines). Infusions were initiated and completed at 0 and 120 hours, respectively (arrows). Inserts: periods of initiation and cessation of dextrose or sham treatments. *Significantly (P < 0.05) different than values measured immediately before the onset of dextrose infusion. +Significantly (P < 0.05) different from values in control group.
discontinuing the dextrose infusion, plasma glucose concentration began to decrease rapidly, reaching a nadir 40 minutes after the end of infusion.

Plasma IRI concentration increased immediately after the onset of dextrose infusion and was greater than baseline concentration from 40 minutes to 60 hours (Figure 1). Mean peak values approximately 16 times as great as baseline values were observed from 90 minutes to 6 hours. After declining at 12 hours, mean plasma IRI concentration plateaued until 60 hours; thereafter, plasma IRI concentration continued to decrease and remained low at all sampling times after dextrose infusion was discontinued. Plasma IRI concentration was higher in dextrose-treated cows than in sham-treated cows from 10 minutes to 72 hours after the onset of dextrose infusion.

Plasma P concentration began to decrease shortly after the onset of IV dextrose infusion, mirroring the increase in plasma glucose concentration (Figure 1). By 12 hours, plasma P concentration had decreased to less than baseline values. The nadir in plasma P concentration was observed at 24 hours, which was 18 hours later than the peak in plasma glucose concentration. Plasma P concentration remained less than baseline value until 36 hours and then began to increase; plasma P concentration was numerically but not significantly less than baseline value at all remaining sampling times until 96 hours. Plasma P concentration was lower in dextrose-treated cows than in sham-treated cows from 6 to 36 hours and at 72 and 108 hours. Within minutes after discontinuing the IV dextrose infusion, plasma P concentration began to increase, peaking 6 hours later; peak values were higher than values at the end of the infusion and occurred approximately 5 hours later than the nadir in plasma glucose concentration. Plasma P concentration took longer to stabilize after the end of infusion than did glucose concentration, and there was more variability among cows.

Plasma concentrations of albumin, Ca, and Cl did not differ between dextrose- and sham-treated cows and were stable over time. Small but significant changes occurred in plasma osmolality (281 ± 1 mosm/kg) and plasma concentrations of Na (135.0 to 141.0 mEq/L) at a few time points associated with frequent blood sampling. Over the course of the treatment period, plasma osmolality in dextrose-treated cows decreased nonsignificantly from 281 ± 1 mosm/kg to a nadir of 276 ± 1 mosm/kg at 108 hours, which resulted in lower plasma osmolality in dextrose-treated cows than in sham-treated cows at 72 hours (277 ± 2 mosm/kg vs 281 ± 1 mosm/kg) and 120 hours (278 ± 0.6 mosm/kg vs 284 ± 2 mosm/kg). Plasma K concentration decreased from 4.2 ± 0.1 mEq/L at baseline to 3.4 ± 0.3 mEq/L and 3.5 ± 0.2 mEq/L at 40 and 90 minutes in dextrose-treated cows and from 4.4 ± 0.2 mEq/L at baseline to 3.5 ± 0.3 mEq/L at 90 minutes in sham-treated cows. Plasma K concentration was lower in dextrose-treated than in sham-treated cows at 40 minutes and at 12, 60, and 85 hours. A numerical increase in plasma K concentration from 4.4 ± 0.1 mEq/L at the end of dextrose infusion to 5.0 ± 0.2 mEq/L 6 hours later was observed, which resulted in higher plasma K concentration in dextrose-treated than sham-treated cows at 1.5 hours (4.1 ± 0.5 mEq/L vs 3.6 ± 0.3 mEq/L) and 6 hours (5.0 ± 0.2 mEq/L vs 4.3 ± 0.2 mEq/L) after cessation of infusion.

No changes were observed in hematologic variables or blood gas values in dextrose- or sham-treated cows. Erythrocytes of dextrose-treated cows appeared morphologically normal.

Urinary glucose clearance remained < 12 mg/12 h in sham-treated cows throughout the study but was increased in dextrose-treated cows at 72 (GEM, 254 mg/12 h; range, 63 to 3,160 mg/12 h) and 84 hours (geometric mean, 563 mg/12 h; range, 116 to 11,891 mg/12 h). Differences between groups were significant at 72, 84, and 96 hours. Urinary P excretion did not change over time, but higher urinary P excretion was found in sham-treated (geometric mean, 33.1 mg/12 h; range, 13.6 to 66 mg/12 h) than in dextrose-treated cows (geometric mean, 2.8 mg/12 h; range, 0 to 7.8 mg/12 h) at 60 hours. Urinary excretion values for Na, K, and Cl did not change over time or differ between treatment groups. Mean ± SD urinary Na excretion over all time points was 764 ± 230 mEq/12 h for dextrose-treated cows and 960 ± 310 mEq/12 h for sham-treated cows. Urinary K and Cl excretions were 2,293 ± 471 mEq/12 h and 484 ± 121 mEq/12 h, respectively, for dextrose-treated cows, and 2,664 ± 750 mEq/12 h and 622 ± 139 mEq/12 h, respectively, for sham-treated cows. Volume of urine collected in a 12-hour period did not change over time or differ between treatment groups. Overall mean urinary production values for dextrose- and sham-treated cows were 6.9 ± 1.7 L/12 h and 8.3 ± 1.5 L/12 h, respectively. Differences in urine osmolality over time or between treatment groups were not observed (overall mean, 926 ± 69 mosm/kg for treated cows and 929 ± 94 mosm/kg for control cows).

Dietary DMI decreased in dextrose-treated cows by 36 hours after the onset of infusion; P intake remained low (approx 25% to 50% less than baseline value) until the last day of the infusion phase (Figure 2). A corresponding 20% to 50% reduction in P intake was observed at most time points from 24 hours to the end of the dextrose infusion phase. After discontinuing the dextrose infusion, DMI and P intake quickly returned to preinfusion values. No changes in DMI or P intake occurred in sham-treated cows over time. Dietary P intake was lower in dextrose-treated cows than in sham-treated cows from 36 hours until the end of the infusion phase.

The reductions in DMI and P intake in dextrose-treated cows were followed by decreased fecal output and fecal P loss (Figure 2). The reduction in daily fecal P loss was evident by 48 hours and persisted until the dextrose infusion was stopped. In contrast, daily fecal P loss did not change in sham-treated cows. Fecal P loss was lower in dextrose-treated cows than in sham-treated cows from 48 hours until 168 hours. Fecal P concentration in dextrose-treated cows decreased from 0.7 ± 0.0% at baseline to 0.5 ± 0.1% at 72 hours and increased to baseline 24 hours after cessation of infusion. Although these changes were not significant, fecal P concentration in dextrose-treated cows was lower than that in sham-treated cows at 72 (0.5 ± 0.1% vs 0.7 ± 0.1%) and 96 (0.6 ± 0.1% vs 0.7 ± 0.1%) hours after discontinuing dextrose infusion.
No differences were observed in salivary P concentration between sham-treated (overall mean, 19.0 ± 3.3 mg/dL) and dextrose-treated (20.7 ± 3.0 mg/dL) cows. Adjustment of these values for DMI did not reveal significant differences between treatment groups, but a numerical difference in overall mean values was apparent (sham-treated cows, 21.6 ± 3.4 mg/dL; dextrose-treated cows, 16.9 ± 3.1 mg/dL). Saliva-to-plasma P concentration ratio was similar for sham- and dextrose-treated cows at all time points (overall means, 5.9 ± 0.7 and 6.0 ± 2.0, respectively). No differences were observed in salivary osmolality (257 ± 11 mosm/L vs 256 ± 13 mosm/L) or salivary concentrations of Na (140 ± 8 mEq/L vs 137 ± 9 mEq/L), K (12.7 ± 3.2 mEq/L vs 13.0 ± 2.0 mEq/L), or Cl (44 ± 3 mEq/L vs 45 ± 3 mEq/L) between sham- and dextrose-treated cows.

Mean daily milk yield was approximately 15 kg/12 h at the start of the dextrose and sham treatment periods (Figure 3). Milk yield increased immediately in dextrose-treated cows from 15.2 ± 1.6 kg/12 h before treatment to 17.3 ± 2.2 kg/12 h by 12 hours after onset of treatment. This was followed by a progressive decrease in milk yield, which decreased to less than baseline value at 108 hours after onset of infusion. Compared with sham-treated cows, milk yield of dextrose-treated cows was higher at 12 hours and lower from 96 hours to 144 hours and at 168 hours. Despite differences in milk yield, milk P loss every 12 hours did not differ between sham- and dextrose-treated cows and remained stable over time (14.3 ± 1.8 g/12 h and 14.9 ± 1.0 g/12 h, respectively).

Cows remained healthy throughout the trial. Low plasma P concentration was not associated with recumbency or obvious weakness. However, pica was observed at 12 to 24 hours after the onset of infusion in the 2 cows with the lowest plasma P concentration (1.6 and 1.8 mg/dL), as evidenced by licking of the concrete components of the tie stall and chewing on the IV line. Pica lasted approximately 12 hours and disappeared as plasma P concentration began to increase; similar signs were not seen during sham infusion.

Because only 2 cows were available for the feed-matched control study, data were not analyzed statistically. Plasma P concentration in the feed-matched control group appeared to remain stable in the first 12 hours (overall mean, 4.0 ± 0.2 mg/dL) but then decreased continuously to reach a nadir 12 hours before the end of the infusion phase (2.7 ± 0.2 mg/dL). A considerable increase in plasma P concentration occurred after the infusion phase ended, from 2.8 ± 1.1 mg/dL at the end of the infusion phase to 4.7 ± 0.1 mg/dL 6 hours later. By 12 hours after cessation of infusion, plasma P concentration had returned to baseline value (overall mean from 132 to 192 hours after discontinuing fluids, 4.0 ± 0.7 mg/dL). No remarkable changes over time were observed in plasma K concentration (overall mean, 4.2 ± 0.3 mEq/L). Milk yield in the feed-matched control cows gradually decreased from 13.8 ± 0.3 kg/12 h at baseline to 11.6 ± 0.3 kg/12 h at the end of the infusion phase and then increased to baseline value at 168 hours. Plasma glucose and IRI concentrations, as well as all other variables obtained during the feed-matched control treatment, were similar to values obtained in the sham-treated cows at the same sampling times.

**Discussion**

Continuous IV infusion of 50% dextrose (0.3 g/kg/h) to healthy lactating dairy
cows resulted in hyperglycemia and hyperinsulinemia and a marked reduction in plasma P concentration. Other effects of IV dextrose infusion included decreased plasma K concentration, decreased DMI and fecal production, and a transient increase in milk production followed by a sustained decrease. All of these effects were reversed after dextrose infusion was stopped.

The decline in plasma P concentration began within 5 minutes of initiating IV dextrose infusion and was associated with an increase in plasma glucose and IRI concentrations. A shift of P from plasma to the intracellular compartment was strongly suspected because we were not able to identify plausible alternative mechanisms. Phosphorus excretion in urine, saliva, and feces did not change at the onset of dextrose infusion. Although milk production was higher in dextrose-treated cows than sham-treated cows at 12 hours, the amount of P secreted in milk did not change. Decreased dietary P intake as a result of decreased DMI likely contributed to a sustained reduction in plasma P concentration in dextrose-treated cows, as was observed in feed-matched control cows, but could not account for the immediate response. Hyperinsulinemic-euglycemic clamp trials in humans and other animals reveal that insulin increases P influx into skeletal muscle cells, possibly through Na-linked P uptake.11-13 The widely accepted assumption that hyperinsulinemia in humans is responsible for a decrease in plasma P concentration even in the absence of hyperglycemia is supported by observations in which a decrease in plasma P concentration to near baseline concentration at 60 hours.22,23 Humans administered dextrose IV at the same rate as in the study reported here (0.3 g/kg/h) for 5 h/d on 3 consecutive days had a decrease in serum P concentration of 22% to 40% on the first day, 34% to 50% on the second day, and 29% to 35% on the third day.22,23 When IV dextrose is administered continuously to humans at 0.075 g/kg/h for several days, serum P concentration reaches its nadir between 30 and 35 hours,21 which is slightly later than for cows in the study reported here that received a higher infusion rate (24 hours). Much of the dextrose administered to lactating dairy cows is used to support milk production, resulting in lower plasma glucose and IRI concentrations than would be achieved in other species receiving the same dextrose infusion regimen. Also, healthy cows are able to reduce feed intake in response to dextrose infusion. We suspect that the decrease in plasma P concentration might have been more severe or prolonged if cows in the study reported here had been anorectic or nonlactating at the time of dextrose infusion because they could not have limited hyperglycemia by decreasing DMI or using blood glucose for lactose production.

The rate of IV dextrose infusion in the study reported here (0.3 g/kg/h) was higher than recommended for treating dairy cows with ketosis or hepatic lipidosis (0.1 to 0.2 g/kg/h [0.05 to 0.09 g/lb/h]).12 Our goal was to maintain plasma glucose concentration between 100 and 120 mg/dL for at least 24 hours, thereby achieving hyperglycemia without glucosuria. In a pilot study involving healthy lactating dairy cows, 0.2 g/kg/h was not sufficient to achieve hyperglycemia; plasma glucose concentration did not exceed 90
mg/dL. More research is needed to determine the plasma glucose concentration or IRI concentration necessary to alter plasma P concentration in dairy cows. Interestingly, when plasma glucose concentration decreased to 80 mg/dL after 96 hours of dextrose infusion in the study reported here, plasma P concentration returned to the reference range.

A concentrated (50%) dextrose solution was used in the study reported here to keep the infused volume low and minimize plasma volume expansion and diuresis. Diuresis associated with plasma volume expansion alters urinary P excretion in humans. Plasma volume did not change substantially during IV dextrose infusion in the study reported here, as indicated by similar Hct, plasma albumin concentration, and plasma osmolality values in dextrose- and sham-treated cows. Glucosuria, which can also alter urinary P excretion, did not occur with the exception of 1 dextrose-treated cow that developed transient glucosuria near the end of the infusion period. Increased urinary P excretion accompanied glucosuria in that cow. Otherwise, diuresis did not occur during IV dextrose infusion, as indicated by stable urine volume and urine osmolality.

Excretion of P in feces and saliva did not change substantially in response to hyperglycemia or hypophosphatemia in the study reported here. Fecal production decreased as a consequence of reduced DMI, resulting in a concurrent decrease in fecal P loss. Fecal P concentration was lower in dextrose-treated cows than in sham-treated cows near the end of the infusion phase, suggesting an adaptive increase in intestinal P absorption. The less pronounced and slightly delayed increase in plasma P concentration in feed-matched control cows, compared with dextrose-treated cows, after the end of treatment suggested that a rapid return to normal feed intake contributed considerably, but not entirely, to the postinfusion increase in plasma P concentration in dextrose-treated cows. Oral supplementation of P to cows increases plasma P concentration within 2 hours. Analysis of saliva samples did not reveal differences between dextrose- and sham-treated cows in osmolality, P, Na, K, or Cl concentrations, suggesting that salivary excretion of electrolytes did not change in response to dextrose infusion or hypophosphatemia. Salivary P concentration reported for ruminants varies widely among studies, ranging from 2 to 60 mEq/L. Salivary P excretion is influenced by parathyroid hormone, calcitriol, and, most importantly, the volume of saliva produced, which accounts for large intra- and intercow variations. Nonetheless, salivary P concentration observed in the study reported here was similar to that reported by Valk et al. Results of adjusting salivary P concentration for DMI to account for assumed changes in saliva volume indicated that salivary P excretion was slightly, but not significantly, reduced in cows with low plasma P concentration.

A decrease in plasma K concentration during and shortly after IV administration of dextrose has been reported in many species and is caused by an insulin-induced intracellular shift of K. This effect has been explained in part by enhanced expression of specific Na-K pump isoforms at high insulin concentrations. In the study reported here, we observed similar changes in plasma K concentration in dextrose-treated and sham-treated cows. The decrease in plasma K concentration that occurred at 40 to 90 minutes in both groups of cows may have been caused by frequent flushing of the catheters and the associated increase in plasma Na concentration. Nonetheless, dextrose-treated cows had significantly lower plasma K concentration at several time points during treatment, compared with the sham-treated cows, suggesting a mild hypokalemic effect of glucose or insulin. On the basis of these data, it could not be determined whether this effect was attributable to hyperglycemia or hyperinsulinemia. Also, we believe that the decreased feed intake in dextrose-treated cows could, at least in part, be responsible for the lower plasma K concentration detected at later stages of the treatment period, although this did not appear to be supported by results of the feed-matched control trial. Whereas insulin appeared to induce an intracellular shift of P and K, the time span during which decreased plasma K concentration was observed in this study was considerably shorter than the period of decreased plasma P concentration. This could possibly be explained by the observation that transient K depletion provokes nearly complete insulin resistance of cellular K uptake. A similar mechanism has not been described for P.

Cows in the study reported here did not have any adverse clinical effects as a result of low plasma P concentration, except for pica. The nadir in plasma P concentration was similar to or lower than values often obtained in recumbent postparturient cows. In other cattle studies, plasma P concentration has been experimentally reduced to values < 1 mg/dL over an extended period without any signs of muscle weakness or recumbency, suggesting that low plasma P concentration might not be a cause of recumbency. Hemolysis or morphologic changes in erythrocytes were not observed during low plasma P concentration in the study reported here, but hemolysis was experimentally induced in cattle by decreasing plasma P concentration to < 1 mg/dL. Pica in cattle has repeatedly been associated with P deficiency, but unequivocal evidence for a causative relationship is not available. Conflicting findings are reported in the literature because some authors have observed pica in P-depleted calves with a plasma P concentration of 3.8 ± 0.55 mg/dL, whereas others have not observed pica in adult cattle with a plasma P concentration < 1 mg/dL for an extended period. To our knowledge, it has not been determined whether pica is attributable to whole-body P depletion or to hypophosphatemia, as occurred in the study reported here. The effect of IV dextrose infusion in sick cows that already have low plasma P concentration and reduced dietary P intake would require further investigation. We chose to study midlactation cows initially, rather than periparturient cows, because midlactation cows are metabolically stable, which allowed us to investigate the specific effects of dextrose infusion on P homeostasis with less risk of confounding factors.

Results of the present study suggest that hypophosphatemia developed in response to hyperglycemia or hyperinsulinemia in dairy cows administered dextrose by continuous IV infusion. The reduction in plasma P concentration was not a result of increased urinary or salivary excretion or increased loss in feces or milk.
Lactating dairy cows responded to continuous IV dextrose infusion by decreasing feed intake, which was accompanied by a decrease in milk production and fecal output. All of the physiologic responses were reversed rapidly after discontinuing IV dextrose infusion. No clinical effects of hypophosphatemia other than pica were observed. The decrease in plasma P concentration was most likely the result of an insulin-induced intracellular shift of P followed by a reduction in P intake. Until further investigation is performed, veterinarians should monitor plasma P concentration in cows given dextrose by continuous IV infusion, especially if cows are periparturient, inappetent, or hypophosphemic.

### References


### Lactating Dairy Cows

- **a.** Angiocath, Becton-Dickinson, Franklin Lakes, NJ.
- **b.** T-Port extension set ET04TSR, Braun, Bethlehem, Pa.
- **c.** Angiocath, Becton-Dickinson, Franklin Lakes, NJ.
- **d.** Extension set 30”, Abbott Laboratories, North Chicago, Ill.
- **e.** Sterile prepierced resal injection caps, Abbott Laboratories, North Chicago, Ill.
- **f.** Sterile 50% dextrose solution, The Butler Co, Columbus, Ohio.
- **g.** Baxter Health Care Corp, Deerfield, Ill.
- **h.** Foal/Call IV Set 8001, International Win Ltd, Kennett Square, Pa.
- **i.** Baxter flo-gard 6200 IV pump, Baxter Health Care Corp, Deerfield, Ill.
- **j.** BD Vacutainer, Becton-Dickinson, Franklin Lakes, NJ.
- **k.** Hitachi 911, Roche Diagnostics, Switzerland.
- **m.** Coat-a-Count Insulin In-vitro Diagnostic test kit, Diagnostic Products Corp, Los Angeles, Calif.
- **n.** Monoject Lavender Stopper, Becton-Dickinson, Franklin Lakes, NJ.
- **o.** Abbio Cell Dyn 3500, Abbott Park, Ill.
- **p.** Rapidlab 855, Bayer Diagnostics, Tarrytown, NY.
- **s.** Salivette, Sarstedt Inc, Newton, NC.
- **t.** SAS 8th ed, SAS Institute Inc,Cary, NC.