Introduction

At the onset of lactation, the dairy cow must cope with a tremendous increase in both calcium and energy demand by the mammary gland. Cows failing to meet these demands can develop milk fever or ketosis. Though the severe hypocalcemia of milk fever is rather easily treated by intravenous injection of calcium salt solutions, cows that have recovered from milk fever are less productive and more susceptible to other metabolic and infectious diseases (Curtis et al., 1984; Curtis et al., 1983; and Risco et al., 1984). Cows that develop clinical ketosis are also at increased risk of developing left-displaced abomasum and retained placenta (Correa et al., 1993). Bertics et al. (1992) demonstrated that the lack of dry matter intake observed in most cows at calving and the ensuing energy deficit was particularly detrimental in that it stimulated lipolysis and greatly accelerated deposition of fat in the liver on the day of calving. Although dietary manipulations can reduce the incidence of milk fever and ketosis (Block, 1984; Dishington, 1975; Green et al., 1981; and Minor et al., 1998), they are not always practical and their effectiveness is compromised if feed intake declines.

Oral administration of large amounts of calcium salts, to force calcium into the blood by passive diffusion, can be used to increase blood calcium concentration during the periparturient period. Calcium chloride will rapidly acidify the cow's blood and urine; however, it also can cause metabolic acidosis in high or repeated doses, limiting the amount of calcium that can be administered. Additionally, calcium chloride is rather irritating to the cow’s mouth and has been implicated as a cause of ulcers in the mouth, esophagus, rumen, and abomasum in some cows (Wentink and Van den Ingh, 1992).

Several compounds, if administered orally, can serve as glucose precursors in ruminants. Propylene glycol has gained commercial use based on the concept that it has an advantage over common dietary glucose precursors, such as lactate and propionate, in that it is generally not degraded in the rumen and passes into the blood intact (Emery et al., 1967). However, it now appears that a portion of the propylene glycol given to the cow is metabolized within the rumen to propionate (Grunner et al., 1994). They reported increased glucose and insulin, with decreased NEFA and 3-hydroxybutyrate, in response to propylene glycol dosage during feed intake restriction. Results from that study suggested a dose of 296 ml was almost as effective as a dose of 887 ml in reducing lipid mobilization. However, some authors have reported higher intakes (>500 ml) of propylene glycol to be toxic, with symptoms ranging from poor rumen function to incoordination and depression of consciousness (Caple and McLean, 1993; Herdt and Gerloff, 1998; and Radostits et al., 1994).

Recently, calcium propionate has been incorporated into drenches as it provides gluconeogenic propionate in addition to calcium to the cow (Goff and Horst, 1994). Though its effects on blood calcium are not as rapid as with calcium chloride, calcium propionate may have a more sustained action. Oral delivery of 50-100 g of calcium as calcium propionate increases plasma calcium concentrations for several hours in dry cows, suggesting it could prove a useful aid in amelioration of the acute hypocalcemia associated with the onset of lactation in dairy cows. The objectives of this study were to determine the effects of supplying supplemental energy (propylene glycol) or calcium plus energy (calcium propionate) as an oral drench at calving on blood measurements, health events, and milk production in a commercial dairy.

CASE STUDY: Evaluation of Calcium Propionate and Propylene Glycol Administered into the Esophagus of Dairy Cattle at Calving
### TABLE 1: Ingredients and composition of diets.

<table>
<thead>
<tr>
<th>Ingredients:</th>
<th>Cow diets</th>
<th>Heifer diets</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Close Up Dry</td>
<td>Fresh (1-15 DIM)</td>
</tr>
<tr>
<td>Corn silage</td>
<td>4.1</td>
<td>5.4</td>
</tr>
<tr>
<td>Alfalfa hay</td>
<td>4.9</td>
<td>6.2</td>
</tr>
<tr>
<td>Corn</td>
<td>2.0</td>
<td>4.5</td>
</tr>
<tr>
<td>Whole cottonseed</td>
<td>0.5</td>
<td>1.4</td>
</tr>
<tr>
<td>Cottonseed hulls</td>
<td>1.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Protein+fat supplement</td>
<td>0.3</td>
<td>3.4</td>
</tr>
<tr>
<td>DCAD premix</td>
<td>1.8</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**Composition:**

- Crude protein, %: 14.0 18.5 18.0 14.5 18.5 17.5
- NDF, %: 35 27 28 41 27 28
- NFC, %: 41 41 42 32 42 42
- Calcium, %: 1.1 1.0 .8 .7 1.0 .8
- Potassium, %: 1.4 1.4 1.4 1.5 1.4 1.3
- Vitamin A, KIU supplemented/d: 172 215 154 182 118 154
- Vitamin D, KIU supplemented/d: 43 63 53 54 40 53
- Vitamin E, IU supplemented/d: 1861 742 617 3000 467 617

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*Composition:*

1. Ration composition calculated from actual forage chemical analyses. Concentrate and mineral values are those found in NRC tables.

2. Lactation cattle were offered free-choice salt.

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**Materials and Methods**

Holstein cattle were sorted by parity (heifers = first lactation or cows = second or greater lactation) and assigned to treatment. Cows and heifers were managed in similar fashion, but housed in separate pens from the dry period through mid-lactation. Animals were moved from the close-up dry pen into a maternity barn approximately 10 d prior to their projected calving date (or by physical signs of an early calving). Diets are described in Table 1. Rations were delivered as a complete total mixed ration. Cows were fed a negative dietary cation-anion difference (DCAD) diet formulated to achieve a urine pH of 6.5. Urine pH was measured weekly and DCAD supplement adjusted accordingly. Heifers were fed a traditional close-up ration.

Animals received the assigned drench within 4 h of calving and again 24 h post-calving. Treatments were: 9.5 L water (control); 9.5 L water plus 300 ml (310 g) of propylene glycol (PG); or 9.5 L water plus 0.68 kg calcium propionate (CP; NutroCal®, Kemin Industries, Inc., Des Moines, IA). All drenches were delivered into the esophagus via an esophageal feeder tube connected to a bilge pump (Springer-McGrath Esophageal
Feeder System, McCook, NE). Each PG drench delivered 4.08 moles of glucose precursor per drench (total treatment = 8.16 moles glucose precursor). Each CP drench delivered 146 g calcium and 7.3 moles of glucose precursor (total treatment = 292 g calcium and 14.6 moles glucose precursor). The amount of calcium propionate administered was chosen based on previous experiments by Goff and Horst (1994).

After calving, animals were moved into their respective fresh pen and observed daily for the first 15 d in milk (DIM). Cattle were monitored for visual and behavioral signs of stress (appearance, activity, etc.) and rectal temperatures were recorded daily for early identification of animals requiring further veterinary attention and diagnosis. Cattle were palpated rectally and uterine secretions scored for the presence of metritis between 8 and 15 DIM. Health events in the fresh period were diagnosed by the herdsman or herd veterinarian and recorded for each animal. If cattle had good health and normal temperatures at 15 DIM, they were moved into the appropriate lactation pen. Milk weights were collected at monthly intervals.

Blood samples were collected prior to each drench (calving and 24 h later) and again on d 4 and 10. Samples were collected by jugular or coccygeal venipuncture, refrigerated until transported back to the laboratory (average of 12 h; always <23 h), centrifuged, and the serum was harvested and frozen (-20°C) until subsequent analyses. Serum determinations included calcium, magnesium, glucose, and non-esterified fatty acids (NEFA). Serum calcium and magnesium concentrations were determined by atomic absorption spectrophotometry (Perkin-Elmer Corp., 1965). Serum β-hydroxybutyrate (Williamson and Mellanby, 1974), glucose (Trinder, 1969), and NEFA (Johnson and Peters, 1993) were determined colorimetrically.

Statistical analyses of data (for blood and milk) were performed by analysis of variance using the GLM procedures of SAS® (SAS Institute, 1998) with animals blocked by parity. Experimental model included age, drench, and age*drench interaction. Monthly milk weights were grouped into periods for statistical purposes, according to calving schedule: Period 1 includes milk weights obtained during the first test in lactation, Period 2 includes milk weights obtained from the second test in lactation, etc. The model for blood analyses included age, drench, time, and any interactions. Means of independent variables found to be significant in the experimental model were separated by use of a Duncan’s post-hoc test. Chi-square analysis was used to assess the effect of treatment on the incidence of retained placenta, clinical ketosis, clinical milk fever, displaced abomasum, and metritis, and to determine significance of group differences.

### Results and Discussion

One hundred sixty nine animals were utilized in this trial. The control group consisted of 22 heifers and 39 cows; the PG treatment group consisted of 21 heifers and 37 cows; and the CP group consisted of 16 heifers and 34 cows. All animals calved within a 53-d window (03/13/00 through 05/05/00). Health events were recorded at calving and continued throughout the trial. Overall incidences were: 1.8% retained placentas; 1.8% ketosis, 0.6% milk fever, 2.4% displaced abomasums, and 4.1% metritis. Clinical milk fever developed in 1 of the 39 cows receiving the control (water) drench; no incidences of clinical milk fever occurred in cows receiving either PG or CP. Treatment had no significant effect on the incidences of retained placenta, ketosis, milk fever, or displaced abomasum (Table 2); however, it would be difficult to discern treatment effects since the incidence of these disorders was very low. One case of ketosis was diagnosed in the control group and 2 cases were diagnosed in the animals receiving CP; no animals receiving the PG drench were diagnosed with ketosis.

The majority of metritis occurred in the control group (6 diagnosed cases out of 61 animals in the control group), with one case in the PG group, and no cases diagnosed in the cattle receiving CP. Chi-square analysis of these data indicated the control group had a significantly greater incidence (P<0.05) of metritis than cattle receiving either the calcium propionate or propylene glycol drench. The average DIM at which metritis was diagnosed was d 8, thus the addition of calcium...
or energy at calving may have improved smooth muscle contraction and hastened uterine involution.

Hypocalcemia has been suggested as a causative factor for displacement of the abomasum (Daniel, 1983). The work of Oetzel (1996) demonstrated that oral calcium chloride treatment to reduce hypocalcemia also reduced displacement of the abomasum. A concern with CP treatment is that the propionate might actually induce displacement of the abomasum. There is some evidence that propionate within the abomasum inhibits contractility of the abomasum, thus increasing the risk of distension and displacement (Breukink, 1991). In this trial, the incidence of displaced abomasum did not increase as a result of CP treatment. Perhaps any possible deleterious effects of propionate in the abomasum were offset by the beneficial effects of calcium entering the blood to maintain abomasal motility.

Previous work reported calcium propionate, delivered as a concentrated drench, raised blood calcium concentration for 4 to 6 hrs after treatment (Goff and Horst, 1994). We did not observe any significant increases in blood calcium level due to treatment. Drenching animals with either PG or CP had no significant effect (P>0.10) on calcium or glucose status of the animals when determined in blood samples taken more than 24 h after treatment (Table 3). There were expected differences in blood constituent concentrations between parity (cows typically have lower blood calcium than heifers at calving). In general, the herd had a low incidence of metabolic disorders and most animals calved within normal parameters of blood Ca, Mg, or glucose concentrations.

The average plasma calcium concentration increased over time and the increase was similar in
### TABLE 3: Plasma levels of calcium, magnesium, glucose, and nonesterified fatty acids (NEFA).

<table>
<thead>
<tr>
<th>Item</th>
<th>Heifers Avg ± SEM</th>
<th>Cows Avg ± SEM</th>
<th>Drench Control ± SEM</th>
<th>PG ± SEM</th>
<th>CP ± SEM</th>
<th>SEM</th>
<th>P level²</th>
<th>Age</th>
<th>Drench</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium, mg/dl</td>
<td>8.59 ± 0.0775</td>
<td>8.38 ± 0.0562</td>
<td>8.57 ± 0.0788</td>
<td>8.41 ± 0.0279</td>
<td>8.46 ± 0.3698</td>
<td>0.0279</td>
<td>0.3698</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium, mg/dl</td>
<td>1.96 ± 0.0342</td>
<td>2.08 ± 0.0248</td>
<td>2.06 ± 0.0348</td>
<td>2.00 ± 0.0001</td>
<td>2.00 ± 0.0433³</td>
<td>0.0001</td>
<td>0.9696</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose, mg/dl</td>
<td>74.25 ± 1.5932</td>
<td>70.14 ± 1.1560</td>
<td>72.08 ± 0.5333</td>
<td>72.00 ± 0.4649b</td>
<td>72.55 ± 0.5424a</td>
<td>0.0391</td>
<td>0.0216</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEFA, meq/L</td>
<td>0.5144 ± 0.0200</td>
<td>0.5126 ± 0.0144</td>
<td>0.5333a</td>
<td>0.4649b</td>
<td>0.5424a</td>
<td>0.0202</td>
<td>0.9409</td>
<td>0.0216</td>
<td></td>
</tr>
<tr>
<td>β-hydroxybutyrate, mg/dl</td>
<td>6.04 ± 0.2754</td>
<td>6.38 ± 0.2015</td>
<td>6.19 ± 0.2828</td>
<td>5.91 ± 0.2828</td>
<td>6.53 ± 0.2828</td>
<td>0.3176</td>
<td>0.3677</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹Drench treatments: Control = 9.5 L water; PG = 9.5 L water + 300 ml propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate. Time 0 and 24 h blood samples were obtained before drench es were administered; averages listed are across all samples.

²Drench means within the same row having different superscripts are significantly different by respective P level listed.

³While there was a statistically significant drench effect (P=0.05), the post-hoc test could not separate differences.

### TABLE 4: Milk production response to oral drenching.

<table>
<thead>
<tr>
<th>Item</th>
<th>Heifers Avg ± SEM</th>
<th>Cows Avg ± SEM</th>
<th>Drench¹ Control ± SEM</th>
<th>PG ± SEM</th>
<th>CP ± SEM</th>
<th>SEM</th>
<th>P level²</th>
<th>Age</th>
<th>Drench</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period 1</td>
<td>32.3 ± 0.9854</td>
<td>47.4 ± 0.7096</td>
<td>38.2 ± 0.9975</td>
<td>41.2 ± 0.0001</td>
<td>40.3 ± 0.0001</td>
<td>0.0001</td>
<td>0.1118</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Period 2</td>
<td>34.2 ± 0.9854</td>
<td>48.7 ± 0.7153</td>
<td>41.1 ± 1.0025</td>
<td>40.7 ± 0.0001</td>
<td>42.6 ± 0.0001</td>
<td>0.0001</td>
<td>0.4528</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Period 3</td>
<td>36.0 ± 1.0546</td>
<td>47.9 ± 0.7889</td>
<td>40.8 ± 1.0727</td>
<td>43.2 ± 0.0001</td>
<td>41.8 ± 0.0001</td>
<td>0.0001</td>
<td>0.3246</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Period 4</td>
<td>36.3 ± 0.9403</td>
<td>43.9 ± 0.6518</td>
<td>39.9 ± 0.9280</td>
<td>40.8 ± 0.0001</td>
<td>39.6 ± 0.0001</td>
<td>0.0001</td>
<td>0.6801</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average kg/d, all periods</td>
<td>35.4 ± 0.8436</td>
<td>47.0 ± 0.5754</td>
<td>39.7a ± 0.8234</td>
<td>42.8b</td>
<td>41.1a,b</td>
<td>0.0001</td>
<td>0.0495</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹Drench treatments: Control = 9.5 L water; PG = 9.5 L water + 300 ml propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate.

²Drench means within the same row having different superscripts are significantly different by respective P level listed.
Figure 1: Effects of experimental oral drench on plasma glucose levels (mean ± SE) in heifers (H) and cows (C). Drench treatments: Control = 9.5 L water; PG = 9.5 L water + 300 ml propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate. Time 0 and 24 h blood samples were obtained before drenches were administered.

Figure 2: Effects of experimental oral drench on plasma NEFA levels (mean ± SE). Drench treatments: Control = 9.5 L water; PG = 9.5 L water + 300 ml propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate. Time 0 and 24 h blood samples were obtained before drenches were administered.
Figure 3a: Effects of experimental oral drench on milk production (mean ± SE) in heifers. Milk production is averaged by period (1, 2, 3, 4). Period designates monthly test weight; average days in milk for heifers are 24, 52, 85, and 114 for Periods 1, 2, 3, and 4, respectively. Drench treatments: Control = 9.5 L water; PG = 9.5 L water + 300 ml propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate.

Both control and treated animals. Plasma calcium concentrations at calving (prior to treatment) were 7.6, 7.7, and 7.9 for control, PG, and CP treated cows, respectively. Plasma calcium concentrations were 8.1, 8.0, and 8.4 mg/dl 24 h later for control, PG, and CP cows, respectively. Ten d after calving, plasma calcium concentrations were 8.9, 9.0, and 8.8 mg/dl in control, PG, and CP treated cows, respectively. Incidence of subclinical hypocalcemia, defined as <7.5 mg/dl plasma calcium (Goff et al., 1996 and Oetzel, 1996), averaged 39%. All plasma calcium concentrations were higher than those reported in previous work (Goff et al., 1996), which may reflect the attention given to maintaining an effective DCAD in this herd.

Similar to calcium, plasma magnesium (Table 3) was affected by age (average plasma magnesium was 1.96 and 2.08 mg/dl for cows and heifers, respectively). There was a significant drench effect (P=0.04), however the biological importance between drench averages may be unimportant. The post-hoc test could not separate differences. Blood magnesium concentrations were marginal (less than 2 mg/dl) in both cows and heifers on d 4 and 10 post-drench, suggesting inadequate dietary magnesium intake in the lactating cow ration or interference with magnesium absorption (Goff, 1998).

Drenching with additional energy, as either propylene glycol or calcium propionate, had no effect on blood glucose. As seen in other studies, all groups calved with elevated plasma glucose concentrations (Figure 1). These higher blood glucose concentrations at calving may be a result of the combination of glucocorticoid release at calving and failure to secrete insulin when blood calcium is reduced (Goff and Horst, 1997). As lactation began, plasma glucose levels declined but remained within normal limits for plasma glucose.

Plasma NEFA responded to oral drench (P=0.02, Figure 2, Table 3), with the animals receiving PG having lower NEFA levels than those receiving either the control or CP treatment (0.533, 0.465, and 0.542 meq/L for the control, PG, and CP treatments, respectively). Plasma β-hydroxybutyrate
was not affected by oral drench (P>0.05, Table 3); as expected, levels were lowest at calving (averaging 4.74, 7.28, and 6.61 mg/dl for the calving, 4 d, and 10 d bleed, respectively). Incidence of subclinical ketosis, defined as >10 mg/dl plasma β-hydroxybutyrate, appeared to be higher in control cows compared to cows receiving PG or CP (15/39, 8/37, and 10/34 subclinical/total cows for control, PG, and CP treatments, respectively). Within these cases, the control group had a greater incidence (P<0.05) of repeat high plasma β-hydroxybutyrate levels (>10 mg/dl) than cows receiving either the PG or CP drench (8/15, 2/8, and 2/10 repeat/subclinical ketotic cows for control, PG, and CP treatments, respectively).

Milk production, averaged across all periods, was 3.1 kg/d greater (P=0.0495) for cattle receiving PG as compared to those receiving the water drench (Table 4). Although not statistically significant, milk production (averaged across periods) was 1.4 kg/d greater for cattle receiving CP as compared to those receiving the water drench. It appeared that heifers received no advantage in milk production from additional calcium, but may have benefitted from additional energy in the form of propylene glycol.

(Figure 3a). Goff et al. (1996) observed no significant increase in milk production in a commercial Holstein herd (multiparous cows only) receiving a lower dose (352 g per drench) of calcium propionate as a paste delivered at calving and again at 24 h post-calving. In this trial, cows receiving a larger dose of CP (680 g per drench) averaged 1.8 kg more milk per d than cows receiving the water control (Figure 3b). Despite the higher dose of calcium propionate, this difference in milk production was not statistically different (P>0.05). Period average DIM for both heifers and cows is listed in Table 5. Days in milk differences between drench treatments were evaluated for potential effects on milk production. Differences were significant for age (heifers vs cows; P<0.05), but there were no differences (P>0.05) across treatments.
Implications

Supplying both additional calcium and energy during the metabolic and feed intake challenge imposed at calving may be of benefit to the cow. Hypocalcemia results in the loss of muscle tone in the gut, uterus, and teat sphincter. This loss of muscle tone, combined with the immunosuppression of excess cortisol at calving, predisposes these animals to displaced abomasum, retained placenta, uterine prolapse, and mastitis. Additionally, the reduced feed intake often noted with hypocalcemic conditions further aggravates the negative energy balance commonly observed in early lactation. Even if clinical milk fever or ketosis is not prevalent in the older cows, as was the case in this herd, the cost of the preventative oral treatment may be justified by potentially higher milk yields and reduced health complications.

Literature Cited


Perkin-Elmer Corp. 1965. Analytical Methods for AtOMIC Absorption Spectrophotometry. Perkin-Elmer, Norwalk, CT.


### TABLE 5: Average and range of DIM by period for milk production.

<table>
<thead>
<tr>
<th>Period</th>
<th>Overall Avg$^2$</th>
<th>Heifers</th>
<th>Cows</th>
<th>P level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Control</td>
<td>PG</td>
<td>CP</td>
</tr>
<tr>
<td>1</td>
<td>21.8</td>
<td>22.4</td>
<td>25.7</td>
<td>24.8</td>
</tr>
<tr>
<td>2</td>
<td>50.0</td>
<td>50.6</td>
<td>54.9</td>
<td>53.2</td>
</tr>
<tr>
<td>3</td>
<td>81.5</td>
<td>82.7</td>
<td>86.9</td>
<td>86.0</td>
</tr>
<tr>
<td>4</td>
<td>112.1</td>
<td>113.0</td>
<td>114.6</td>
<td>114.9</td>
</tr>
</tbody>
</table>

$^1$Drench treatments: Control = 9.5 L water; PG = 9.5 L water + 300 ml propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate.

$^2$Overall average includes both cows and heifers across all treatments.