

One Case of Milk Fever is Just the Tip of an Iceberg

José E.P. Santos, A. Vireira-Neto, R. Zimpel, N. Martinez, C. Lopera, and C. Nelson

**Department of Animal Sciences
University of Florida**



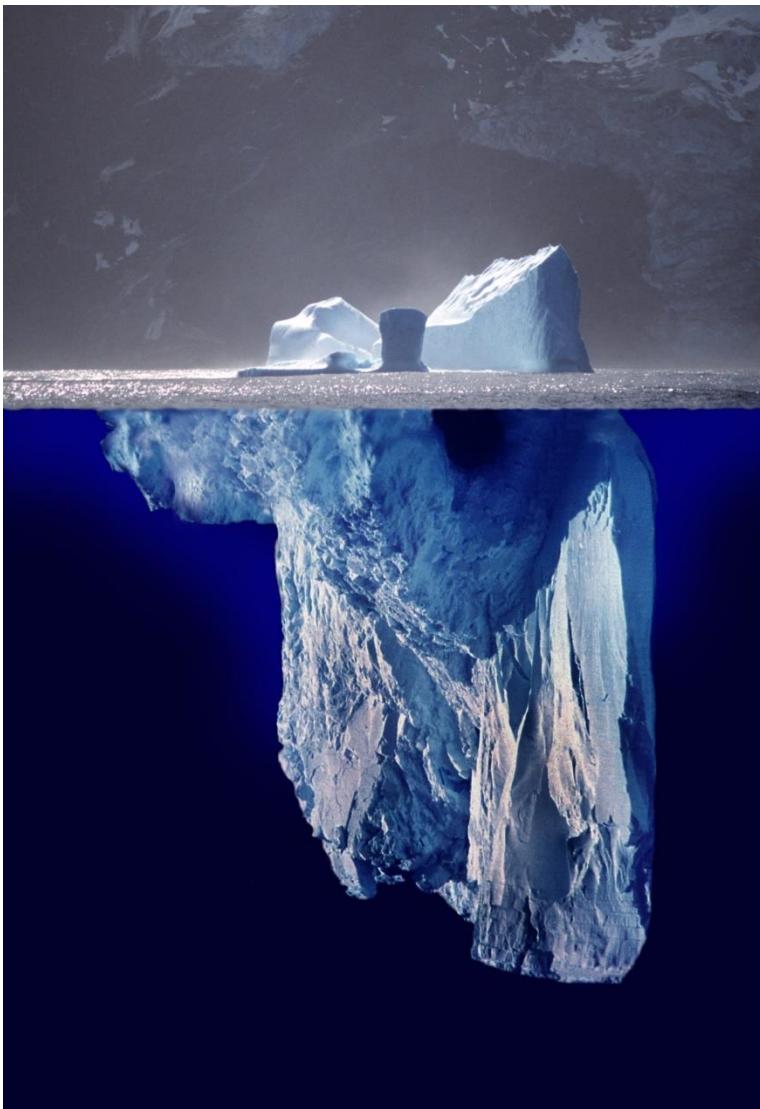
Pictures by Bonnie Mohr <http://www.bonniemohr.com/>

CATTLE CONGRESS 2020
February 24 and 25 at the MCH Herning Convention Center.

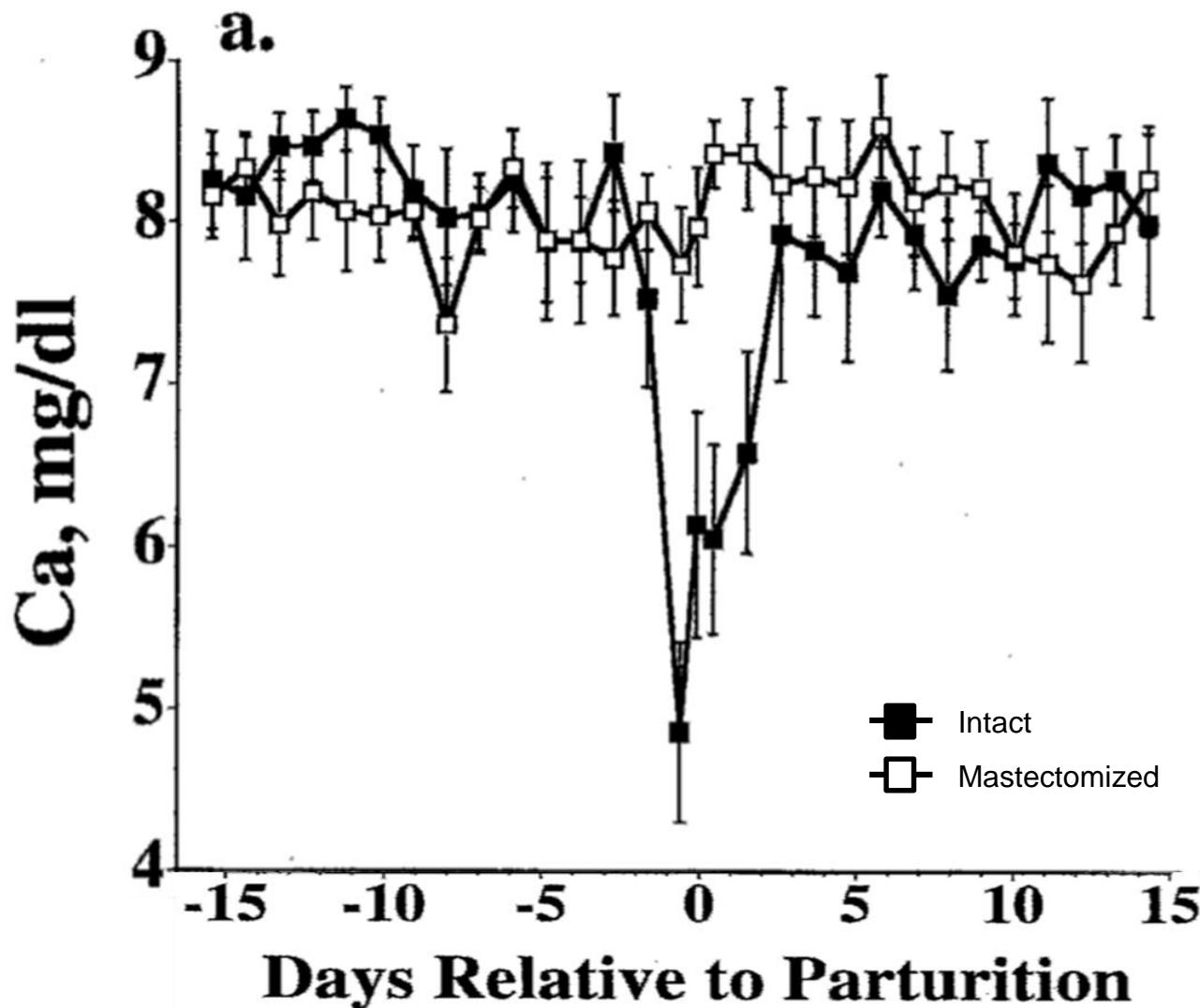


**UNIVERSITY OF
FLORIDA**
Department of Animal Sciences

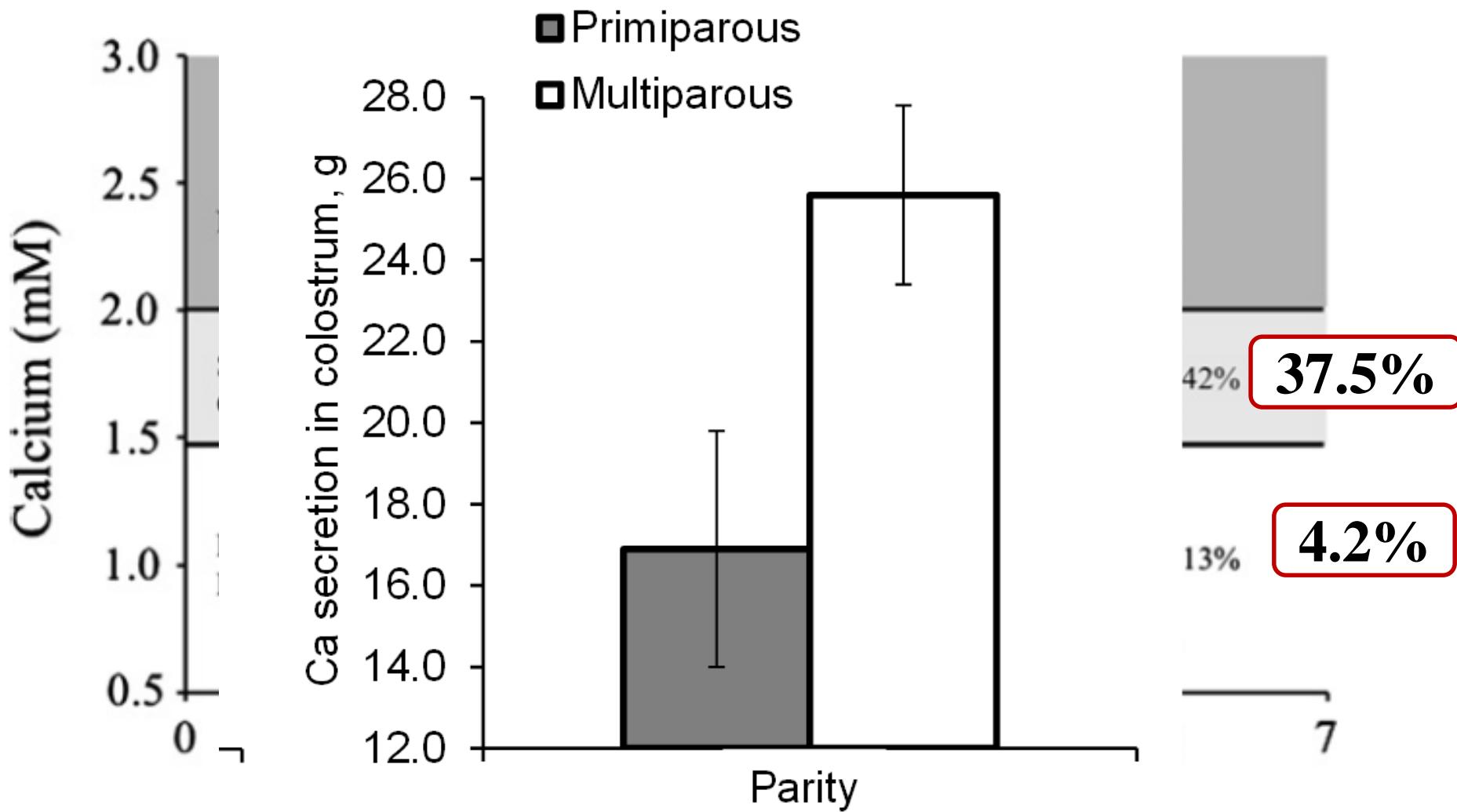
Hypocalcemia in Dairy Cows



Mastectomized Cow



Hypocalcemia in Dairy Cows



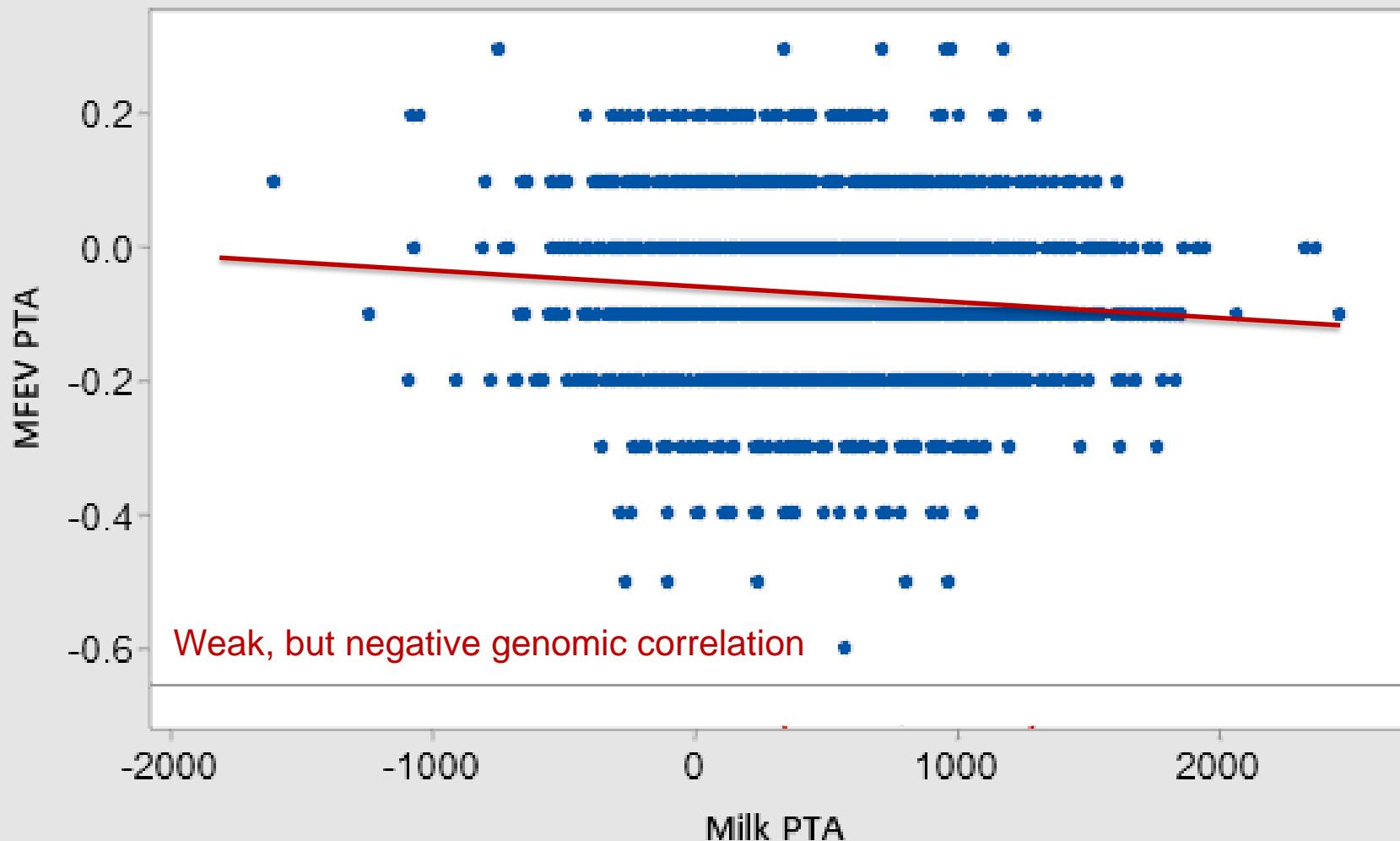
Risk Factors for Hypocalcemia

- ✓ Animal
 - ✓ Older cows (parity)
 - ✓ Jersey breed
 - ✓ Previous lactation milk yield
 - ✓ Previous case of hypocalcemia
 - ✓ Overcondition in the dry period
 - ✓ Previous dry period length
 - ✓ Genetics
- ✓ Nutritional
 - ✓ High K and Na (alkalogenic diets)
 - ✓ High P intake
 - ✓ Low dietary Mg
- ✓ Management/Environment
 - ✓ Inadequate bunk space
 - ✓ Overcrowding

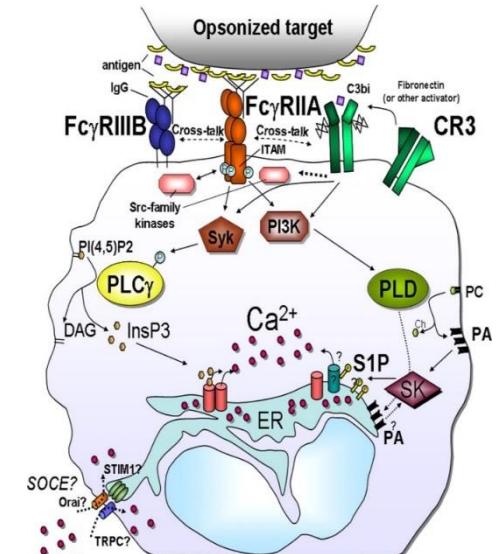
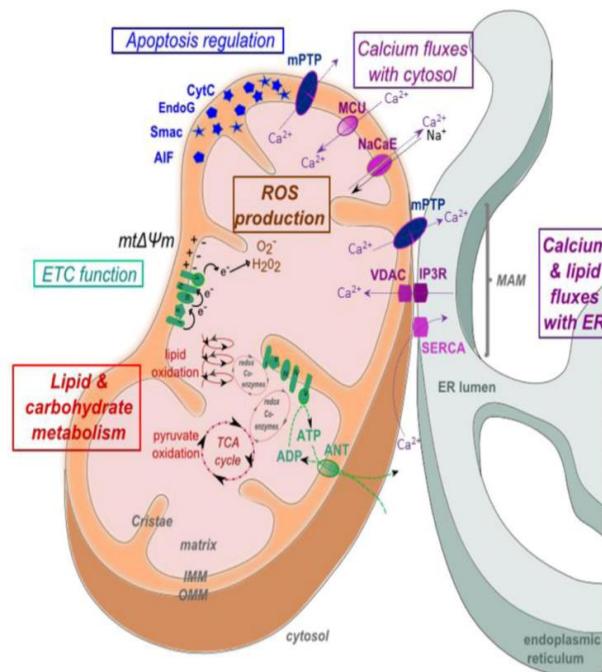


Risk Factors for Hypocalcemia

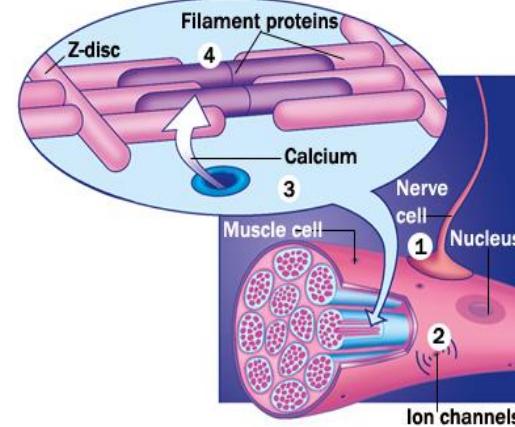
Genomic Correlation Milk and Resistance to Milk Fever in Holsteins
95% CI for Pearson Correlation



Calcium Has Numerous Roles

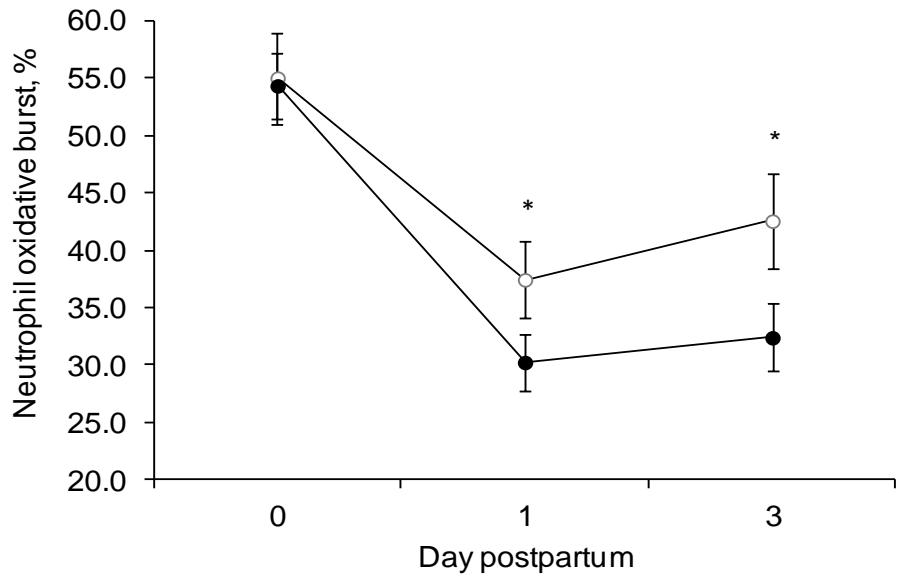
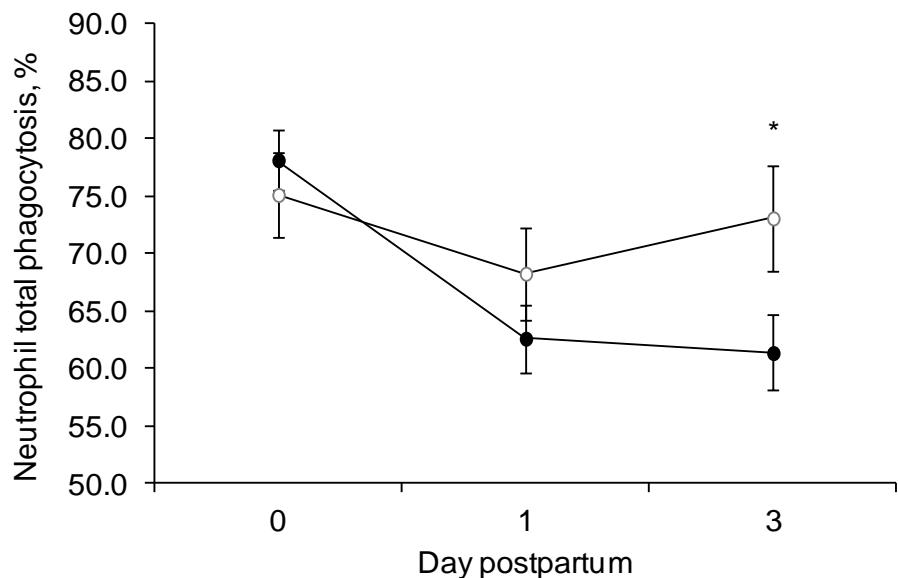
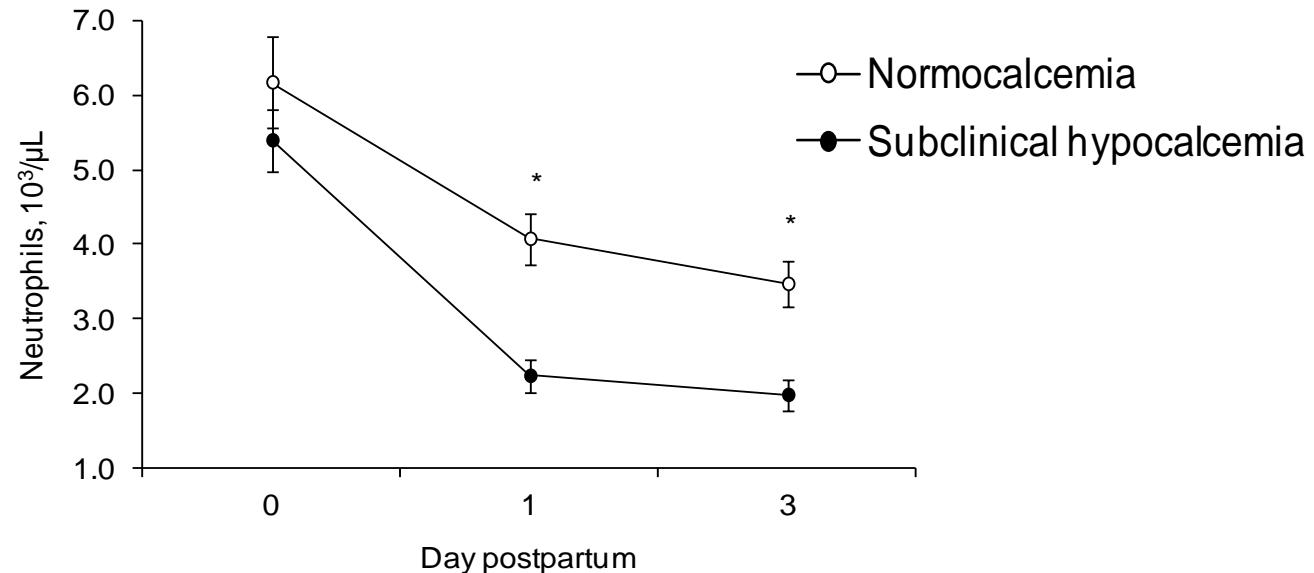


Nunes P , and Demaurex N J Leukoc Biol 2010;88:57-68



Neutrophil Function

* Within a day, $P < 0.05$



Subclinical Hypocalcemia and Metritis

	Subclinical hypocalcemia ¹		Normocalcemia	
	Low Risk	High Risk	Low Risk	High Risk
Metritis, % ^{*,¶}	40.7 (11/27)	77.8 (35/45)	14.3 (4/28)	20.0 (2/10)
Puerperal metritis, % ^{*,¶}	29.6 (8/27)	53.5 (24/45)	0 (0/28)	10.0 (1/10)

*Effect of hypocalcemia ($P < 0.05$),

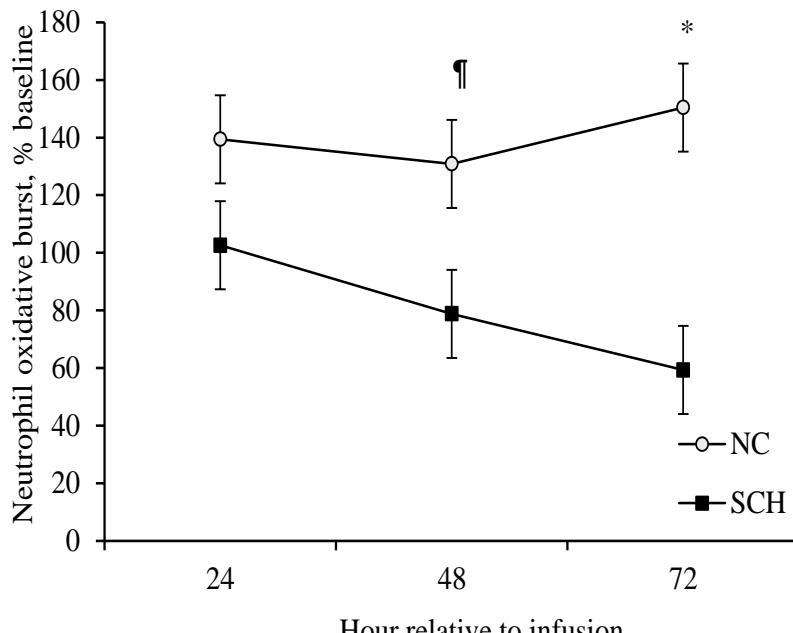
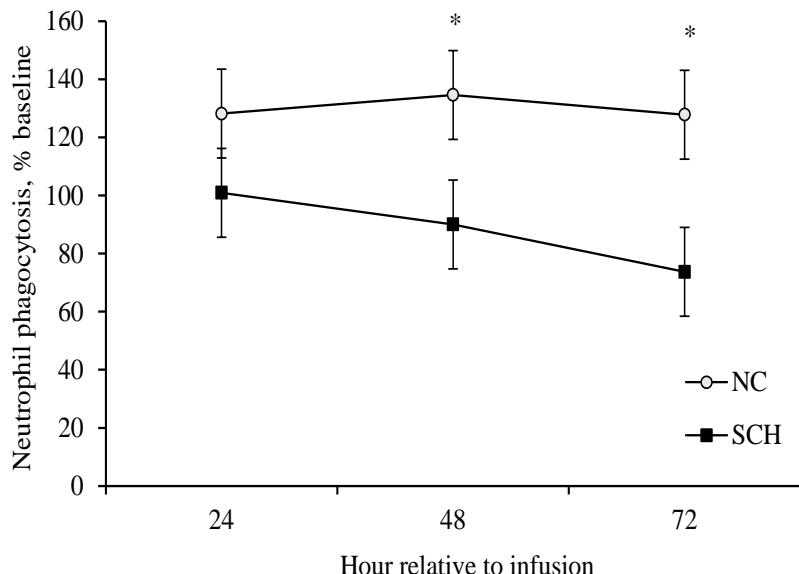
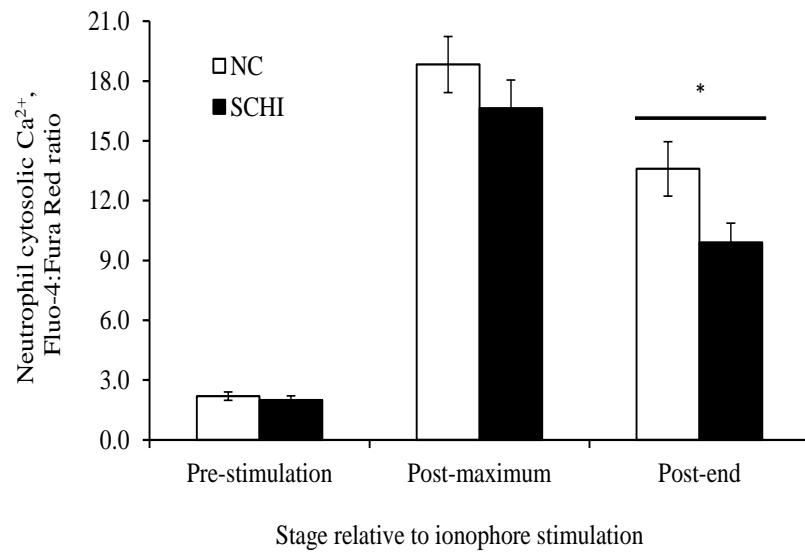
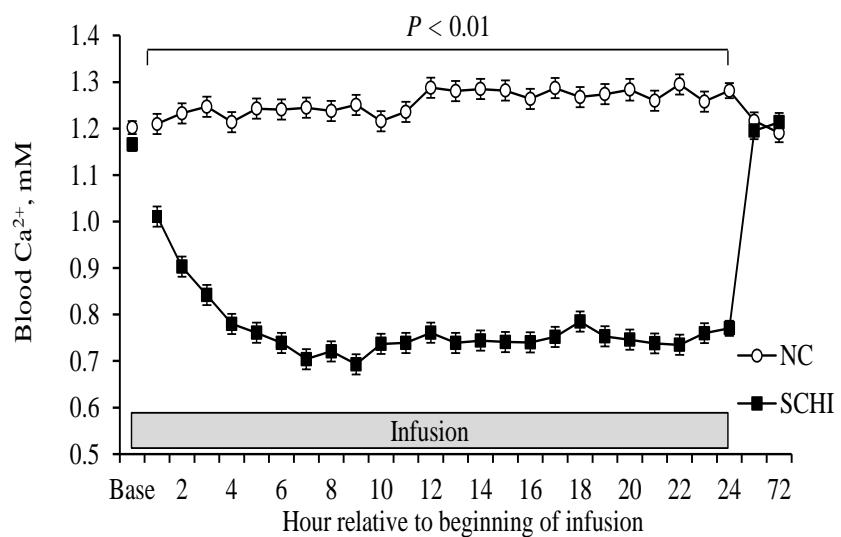
¶ Effect of metritis risk ($P < 0.05$).

¹ Serum Ca ≤ 8.59 mg/dL in the first 3 d postpartum.

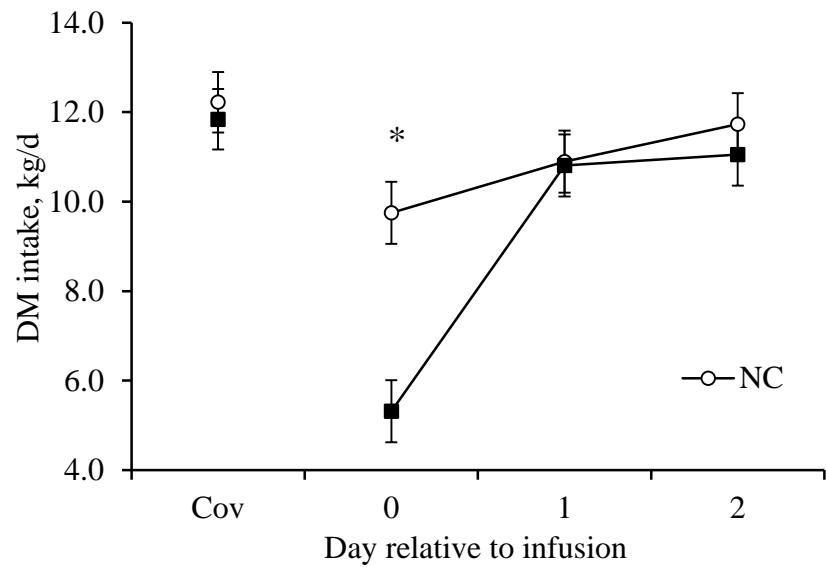
² Puerperal metritis was defined as metritis with presence of fever ($\geq 39.5^{\circ}\text{C}$).



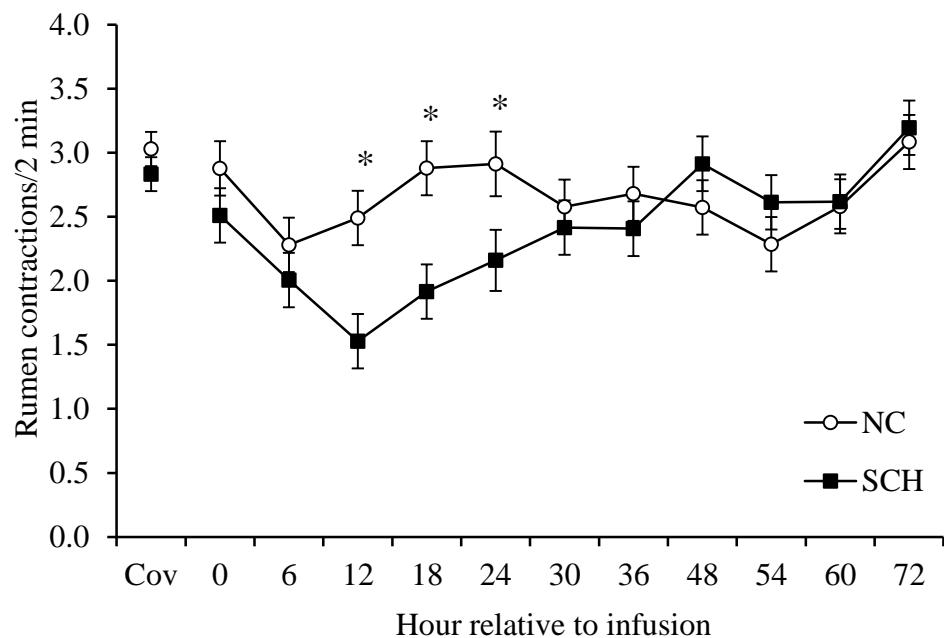
Induced Subclinical Hypocalcemia in Dairy Cows



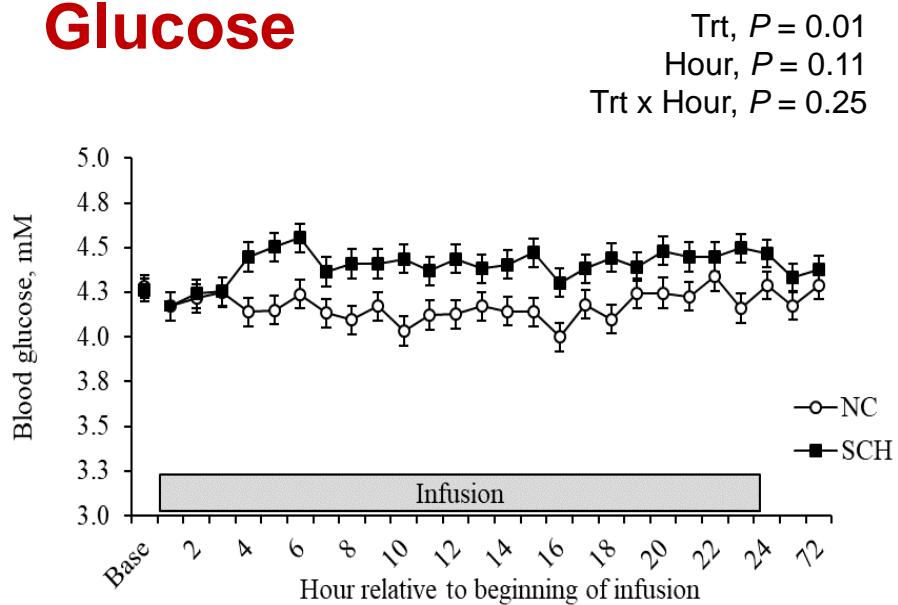
Subclinical Hypocalcemia Reduces DM Intake and Rumen Motility in Dairy Cows



* P < 0.01

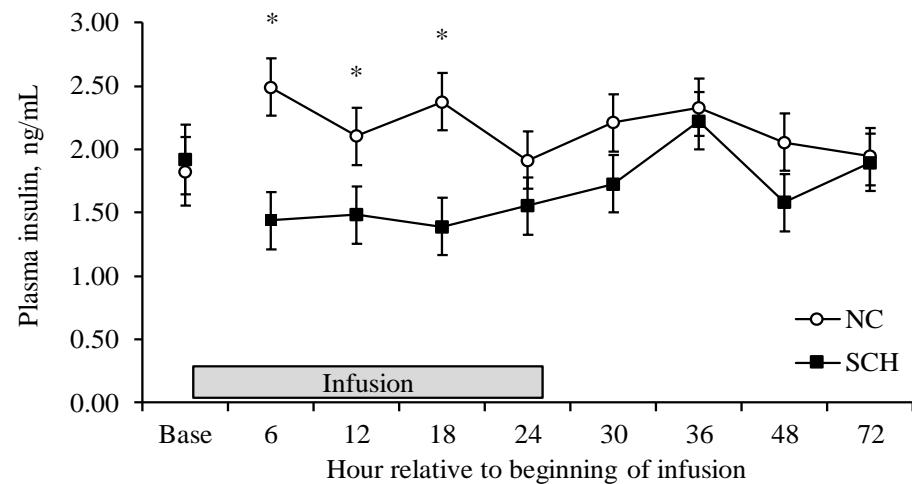


Glucose

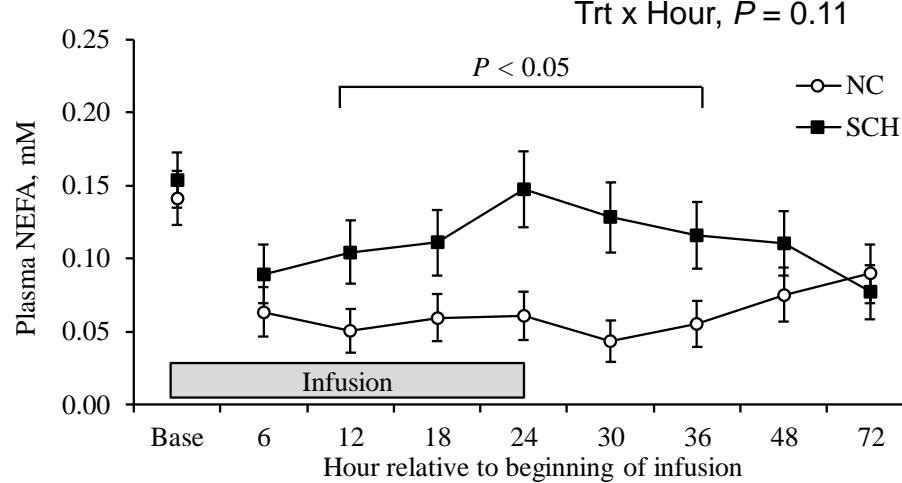


Insulin

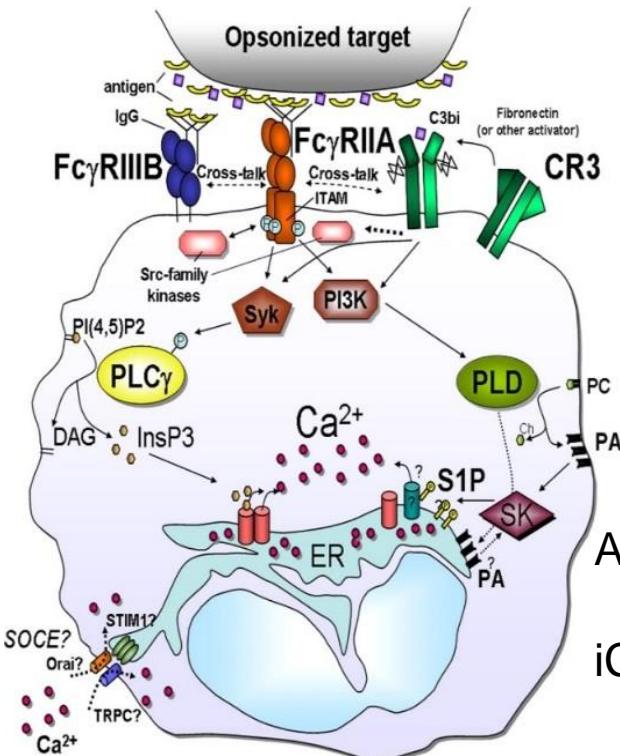
Trt, $P = 0.07$
Hour, $P = 0.05$
Trt x Hour, $P = 0.02$



NEFA



Does Activation of Immune Cells Affect [iCa]?



Blood [iCa]

1.2 mM

Neutrophil [iCa] at resting

85 nM

Neutrophil [iCa] at activation

400 nM

Neutrophils in 1mL of blood

3×10^6

Absolute iCa in 1 mL blood

48,000.00 ng

iCa used by neutrophil activation in 1 mL blood

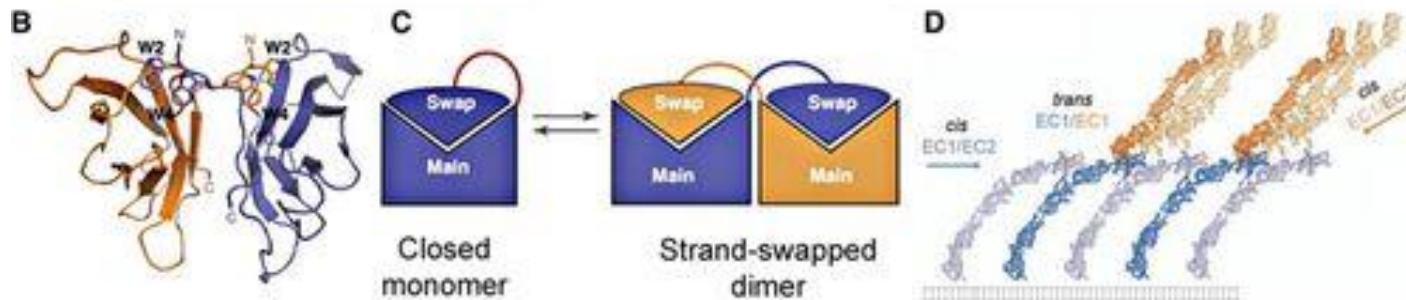
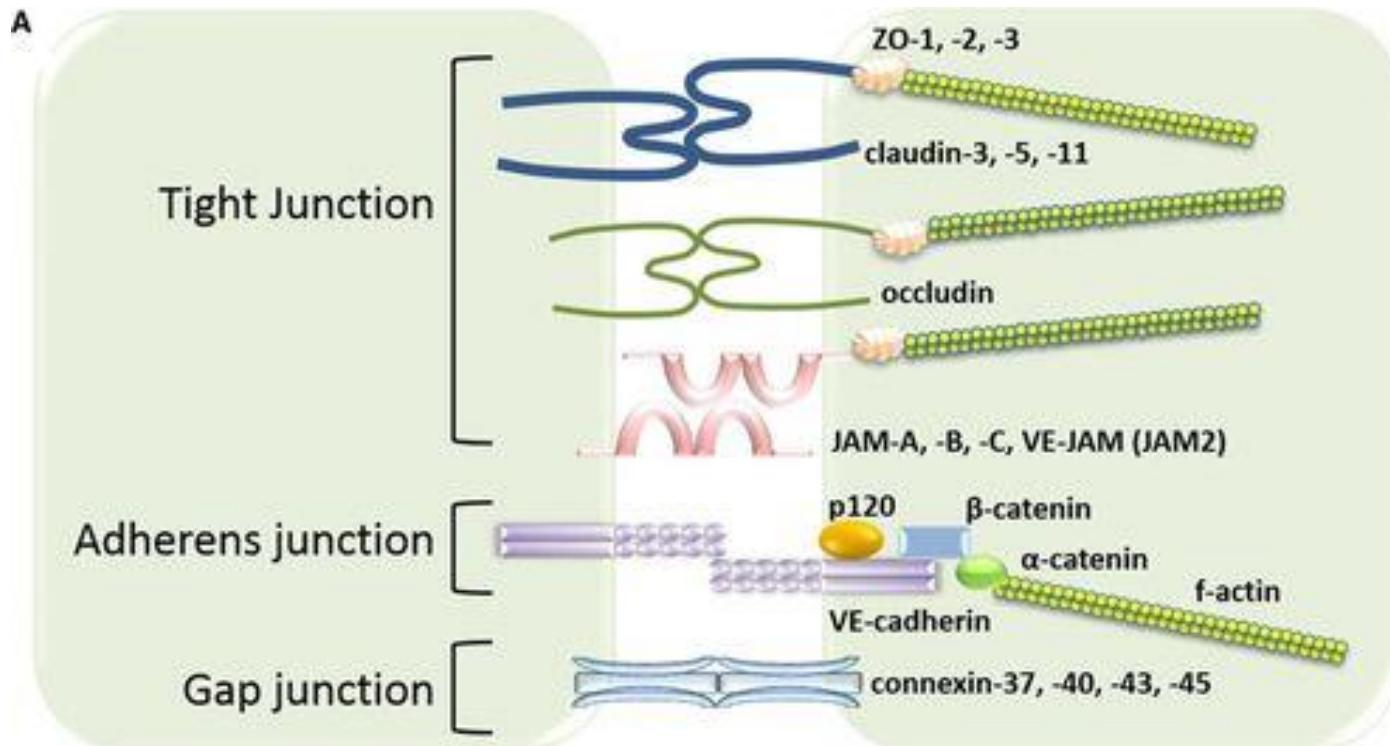
0.03 ng

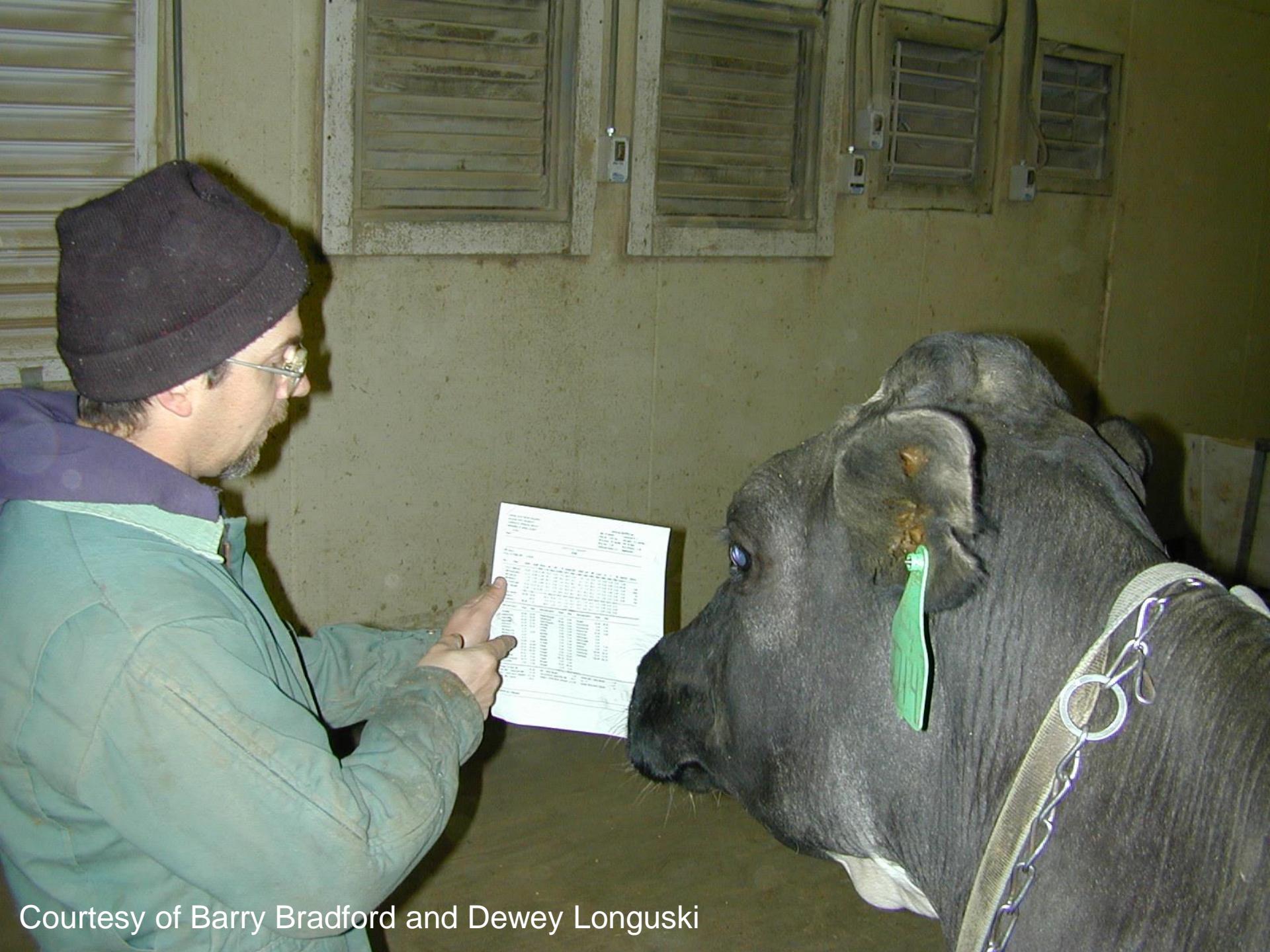
Nunes P , and Demaurex N J Leukoc Biol 2010;88:57-68

Proportion of iCa used upon activation of neutrophils **0.0000695%** of the plasma pool

Vieira-Neto et al. (2020) J. Anim. Sci. submitted

Inflammation Activates TLR4 and Disrupts IEJs Proteins





Courtesy of Barry Bradford and Dewey Longuski

Don't Let Her Choose

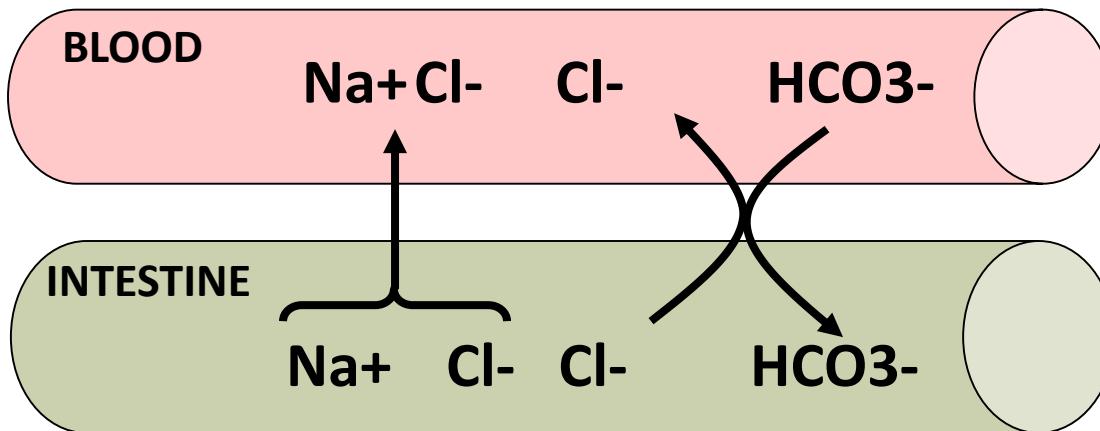


Formulate proper pre-partum diets to reduce the risk of early lactation metabolic diseases

Strategies Available to Reduce the Risk of Hypocalcemia

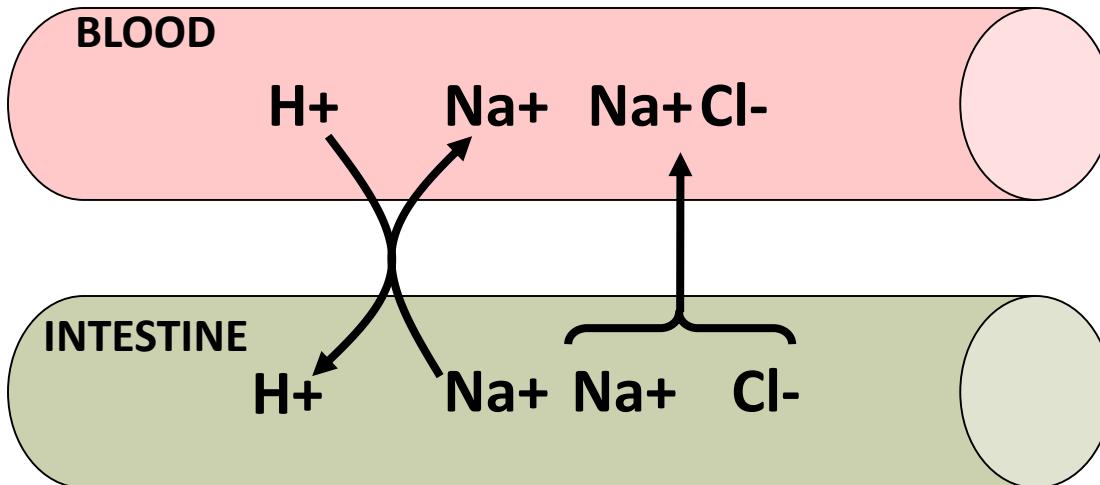
- ✓ Prepartum diets with very low Ca content
- ✓ Reduced intestinal absorption of Ca
- ✓ Altered acid-base status by dietary manipulation
- ✓ Administration of Ca at calving
- ✓ Pharmacological manipulations

How Manipulating the DCAD Affects Blood Acid-Base Chemistry



Negative DCAD with excess of strong anions relative to strong cations

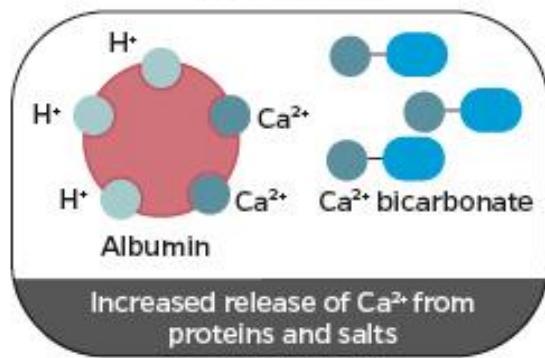
HCO_3 and pH ↓



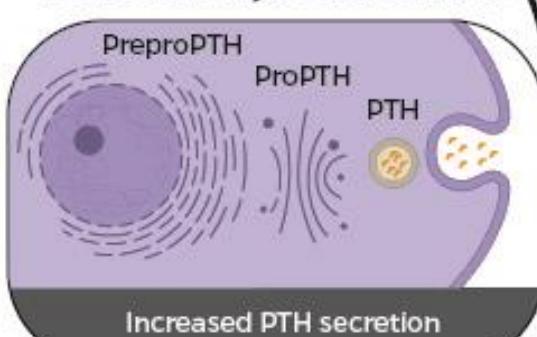
Positive DCAD with excess of strong cations relative to strong anions

HCO_3 and pH ↑

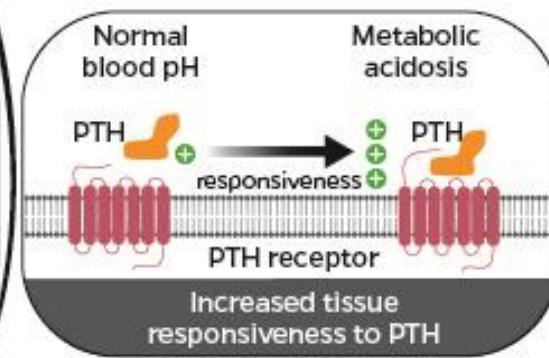
A. Blood



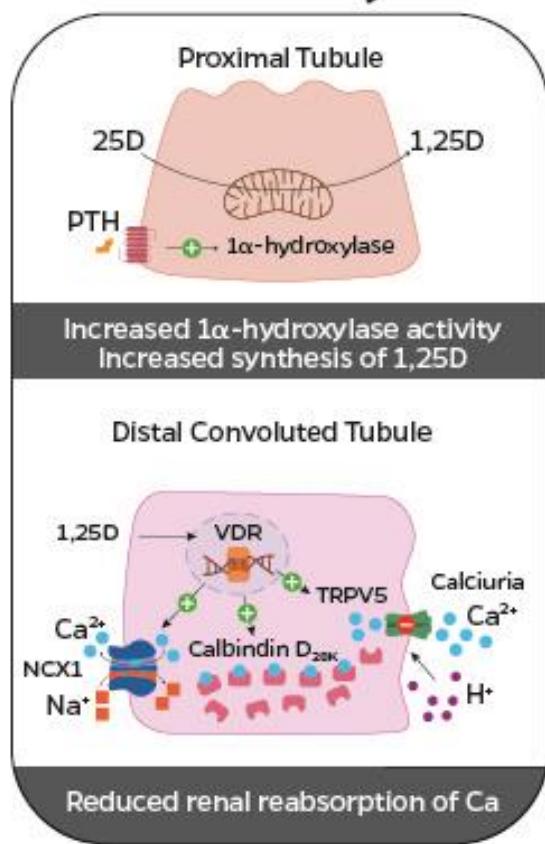
B. Parathyroid Gland



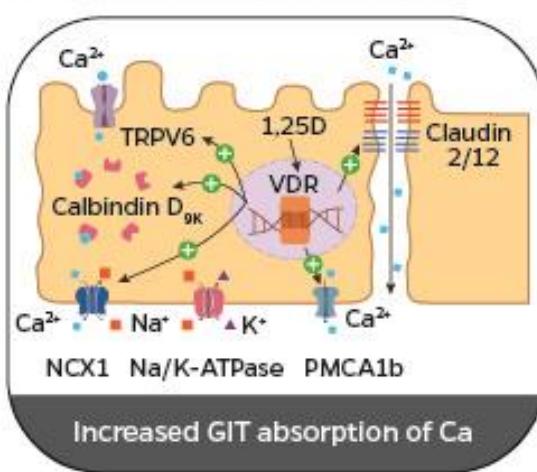
C. Whole Animal



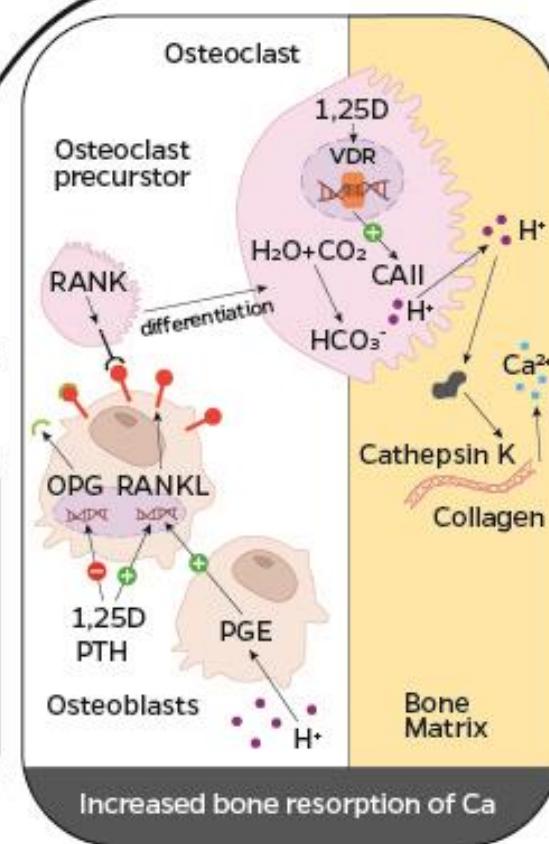
D. Kidney



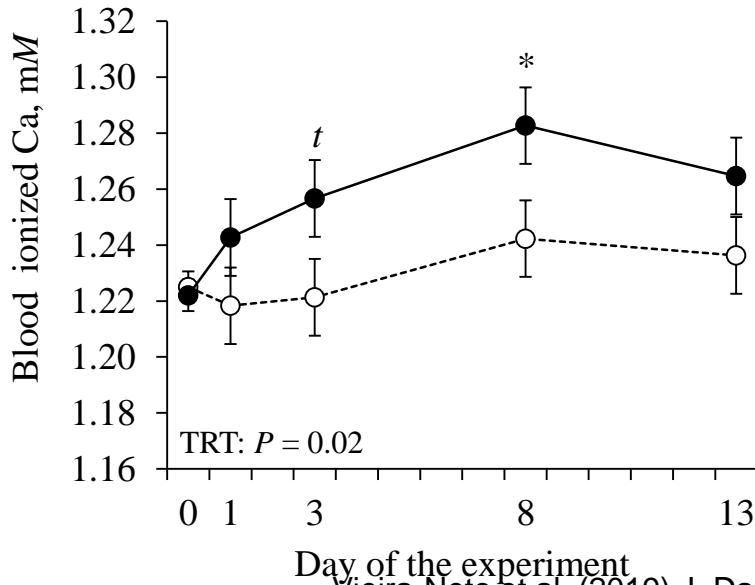
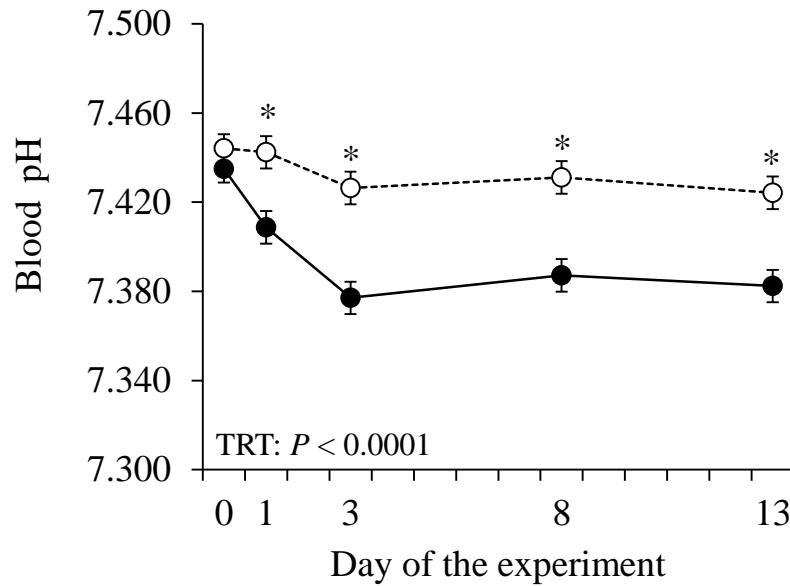
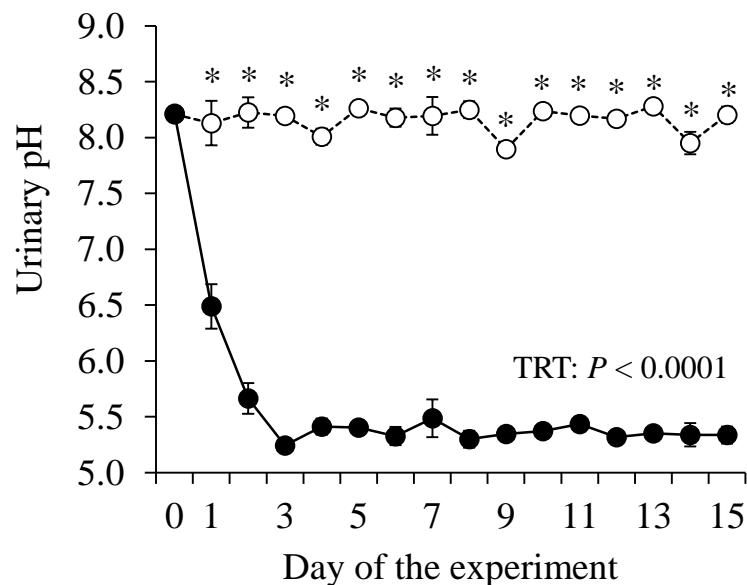
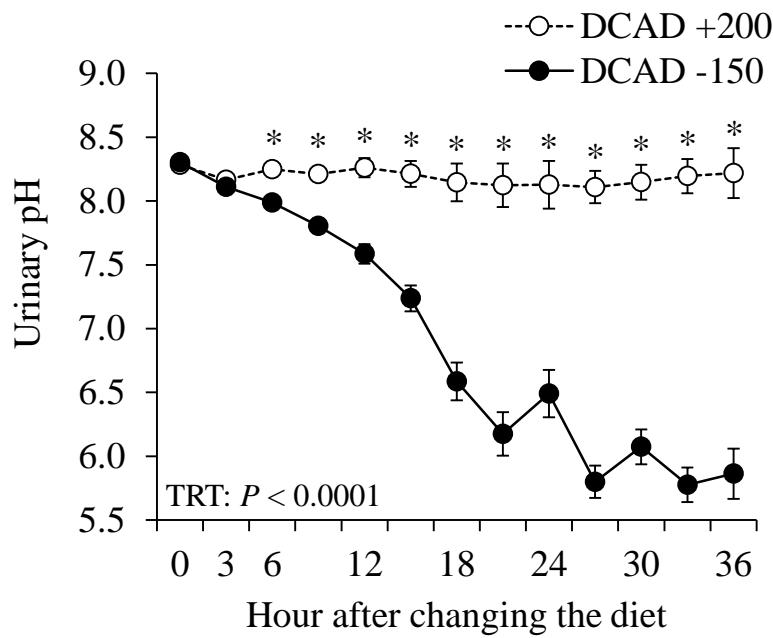
E. Gastrointestinal Tract



F. Bone

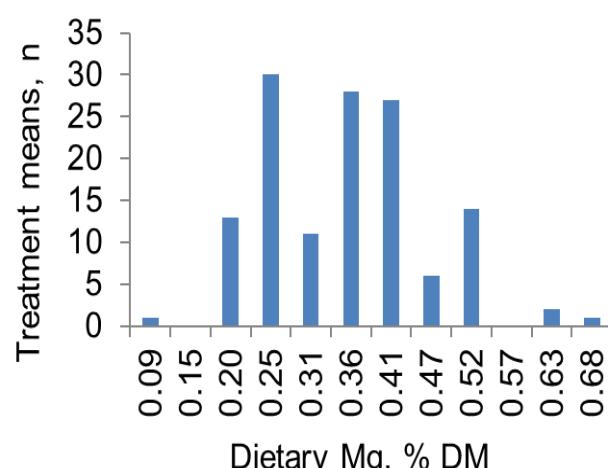
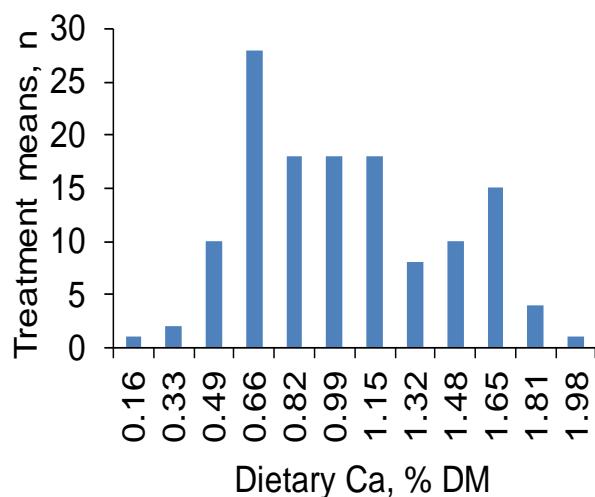
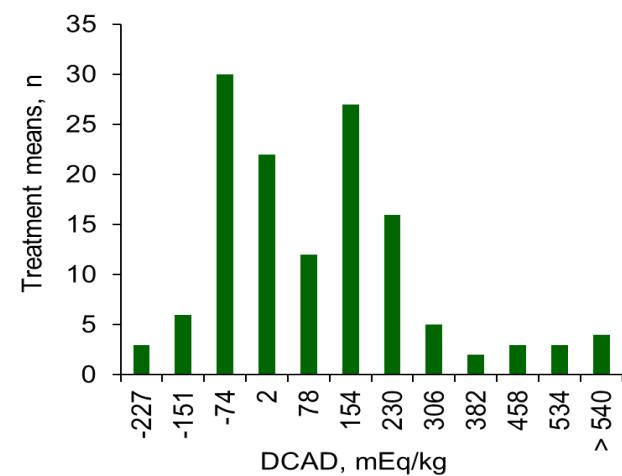


Diet effects on acid-base status

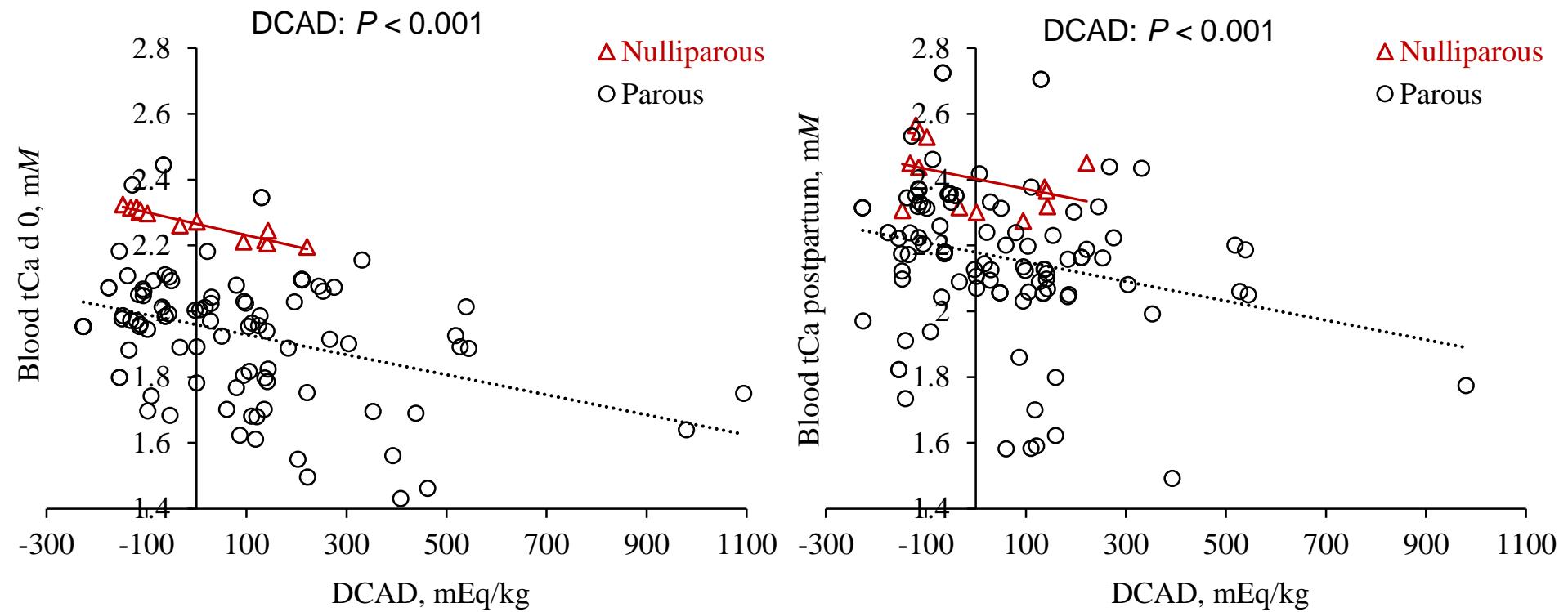


Descriptive statistics of intake of minerals prepartum according to parity group

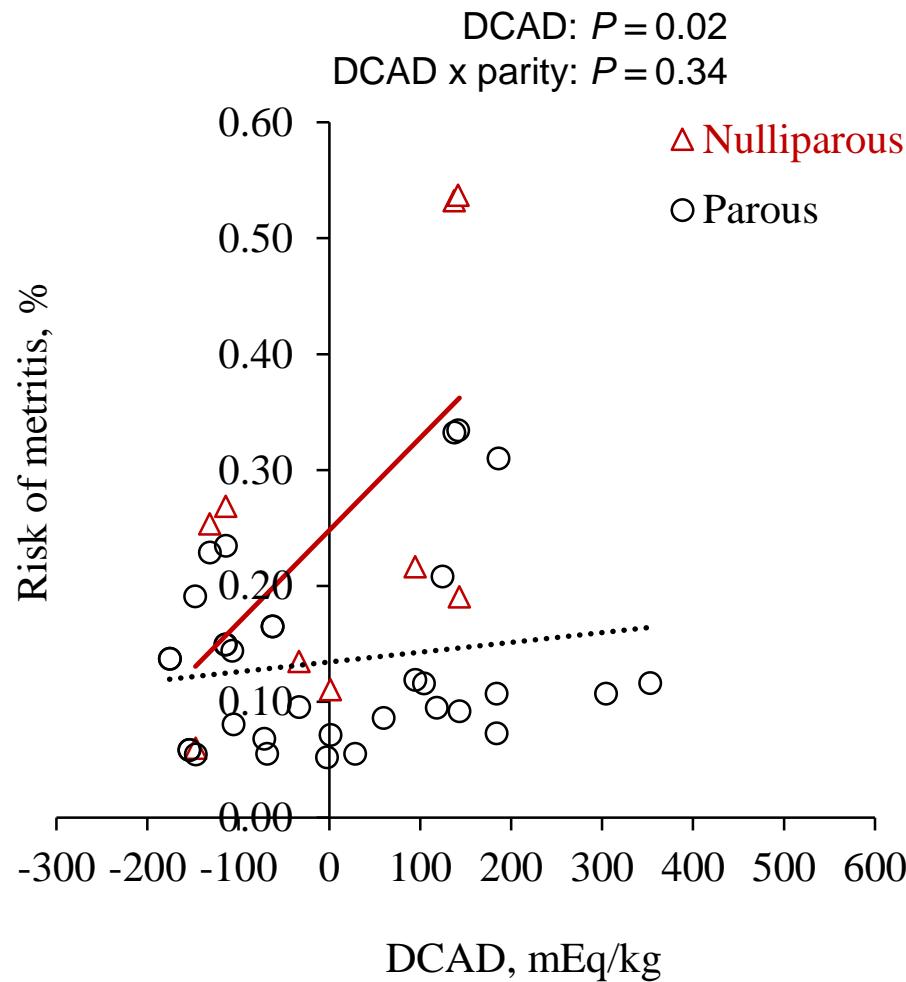
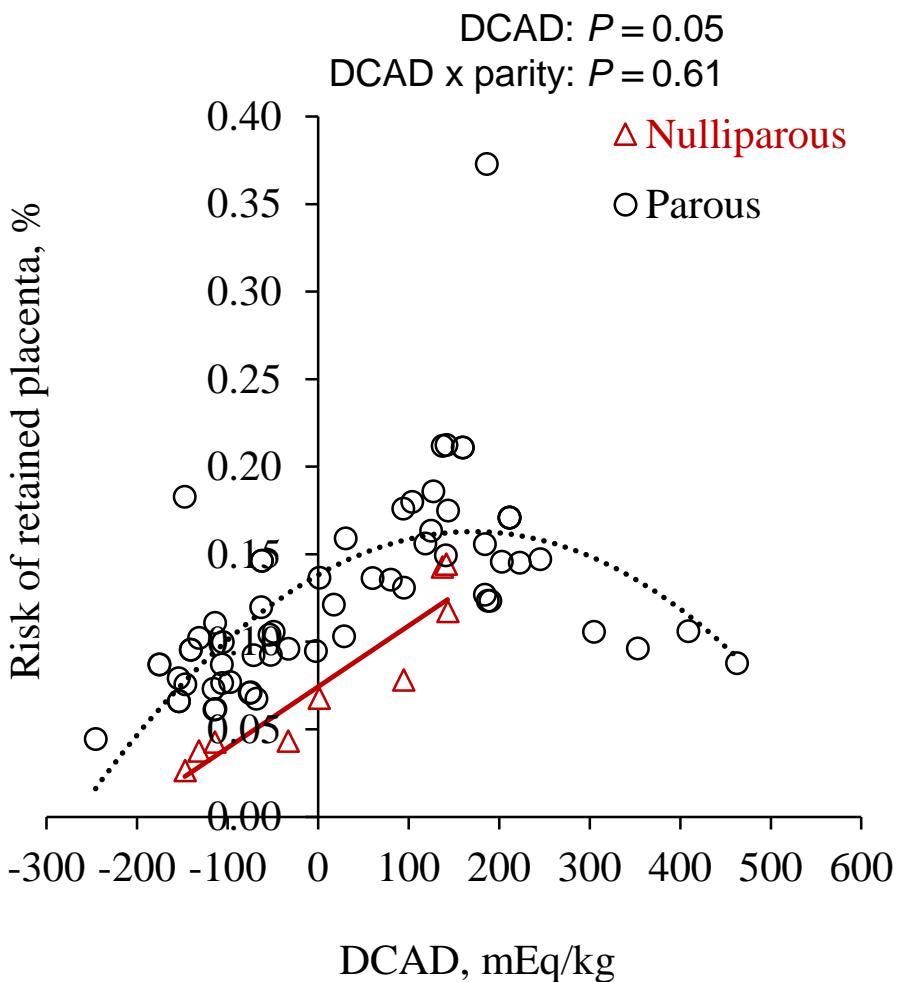
Item	Nulliparous		Parous	
	Mean ± SD	Range	Mean ± SD	Range
Intake, g/d				
Ca	99.2 ± 35.1	46.2 to 166.4	106.6 ± 54.4	9.5 to 272.2
P	35.9 ± 9.4	22.3 to 52.5	44.1 ± 16.2	10.0 to 100.1
Mg	31.7 ± 8.4	21.0 to 44.2	37.5 ± 15.7	10.0 to 87.4
K	134.5 ± 23.4	91.0 to 171.3	161.3 ± 56.2	50.1 to 372.7
Na	18.3 ± 7.1	7.4 to 30.9	20.0 ± 18.0	1.0 to 137.6
S	33.8 ± 17.7	16.4 to 84.5	36.5 ± 17.8	9.9 to 101.5
Cl	73.7 ± 31.6	18.2 to 125.0	74.9 ± 41.0	6.9 to 197.8
DCAD, ² net Eq/d	0.1 ± 1.4	-1.5 to 2.6	0.6 ± 2.2	-2.8 to 9.4



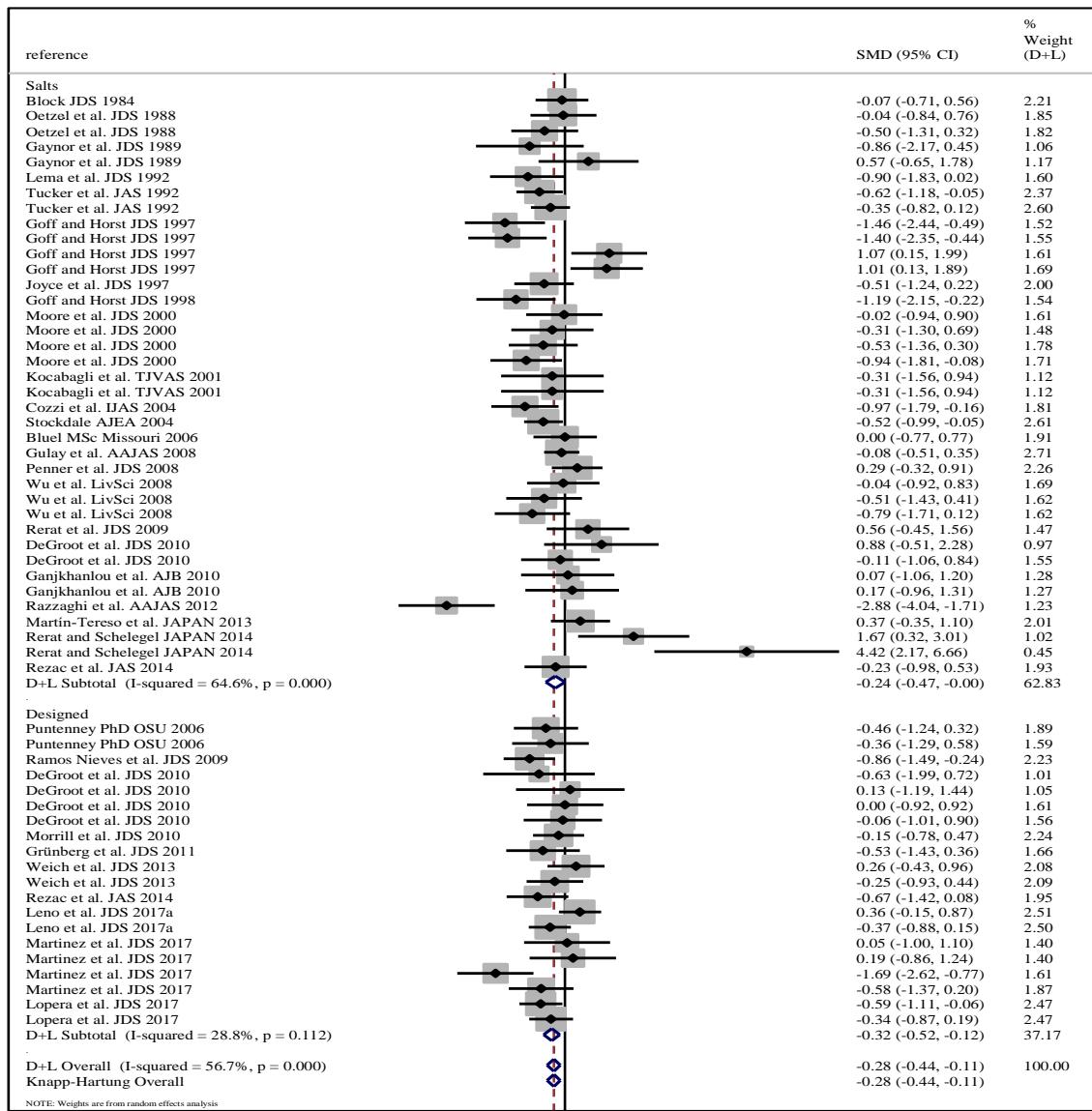
DCAD and Blood [tCa] on the Day of Calving and Postpartum



Effect of DCAD on Risk of Retained Placenta or Metritis



Prepartum DMI

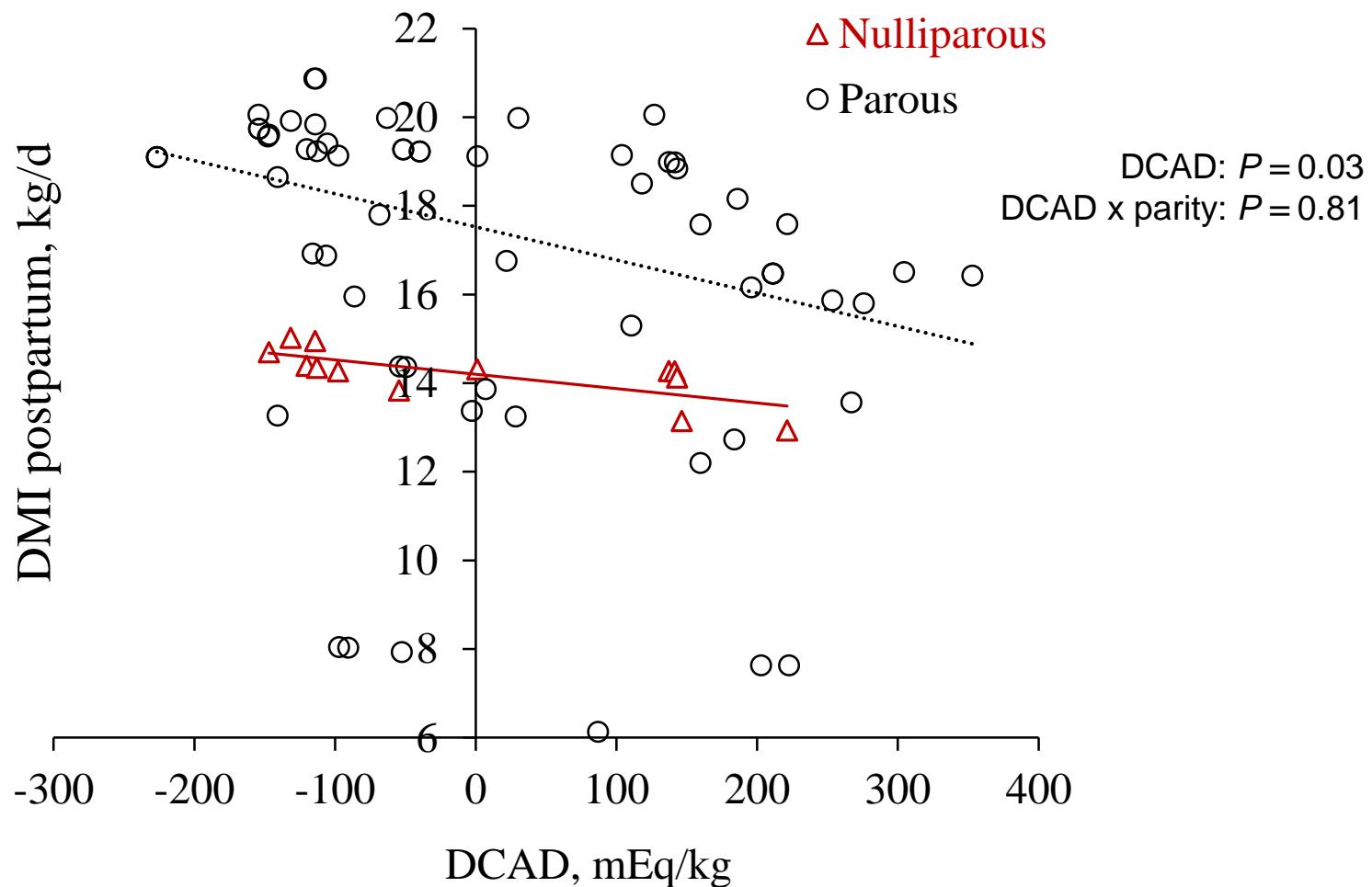


DCAD: $P = 0.02$

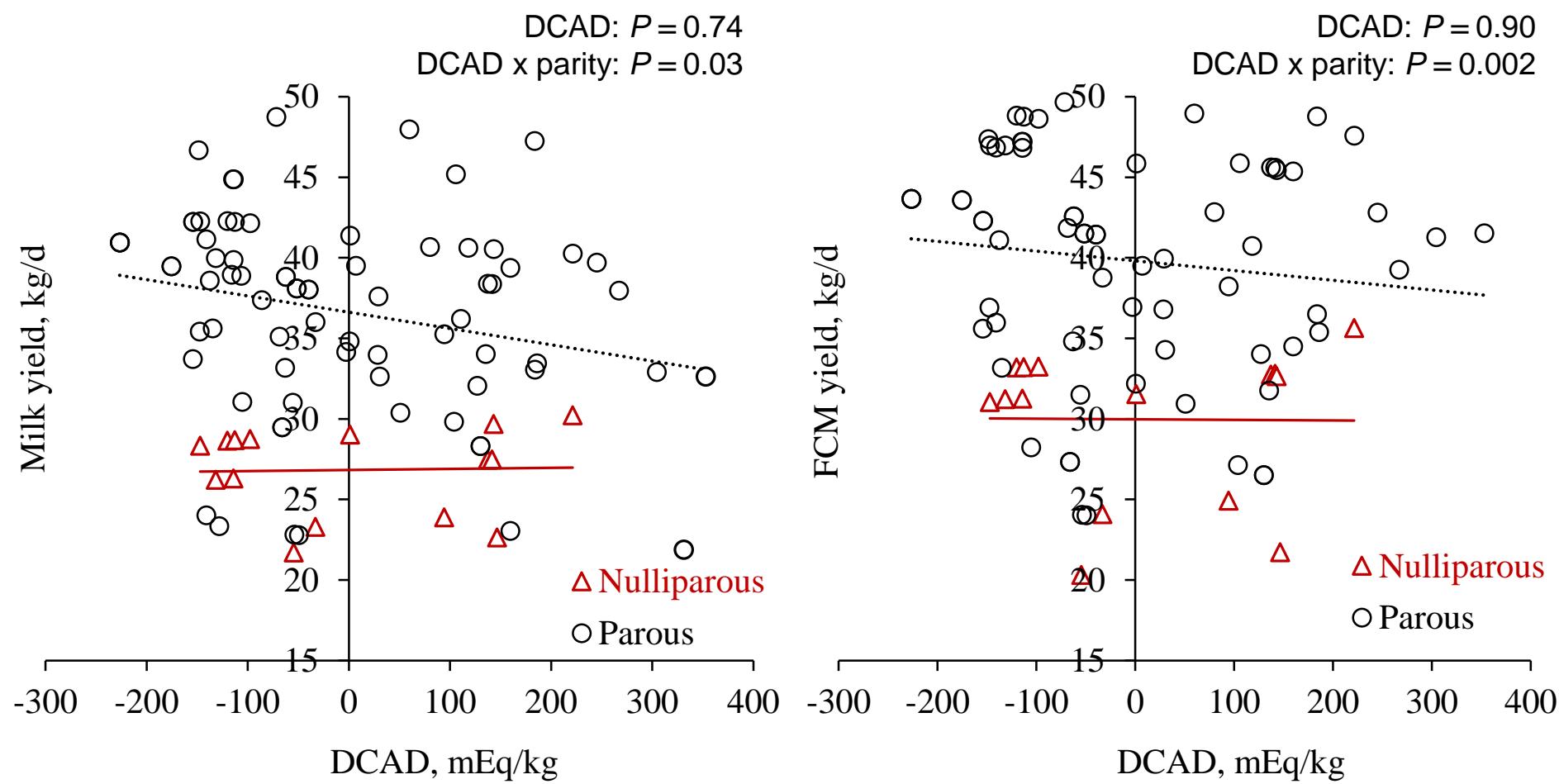
DCAD x type of product: $P = 0.49$

Reduction in 0.5 kg/d
with use of acidogenic
diets

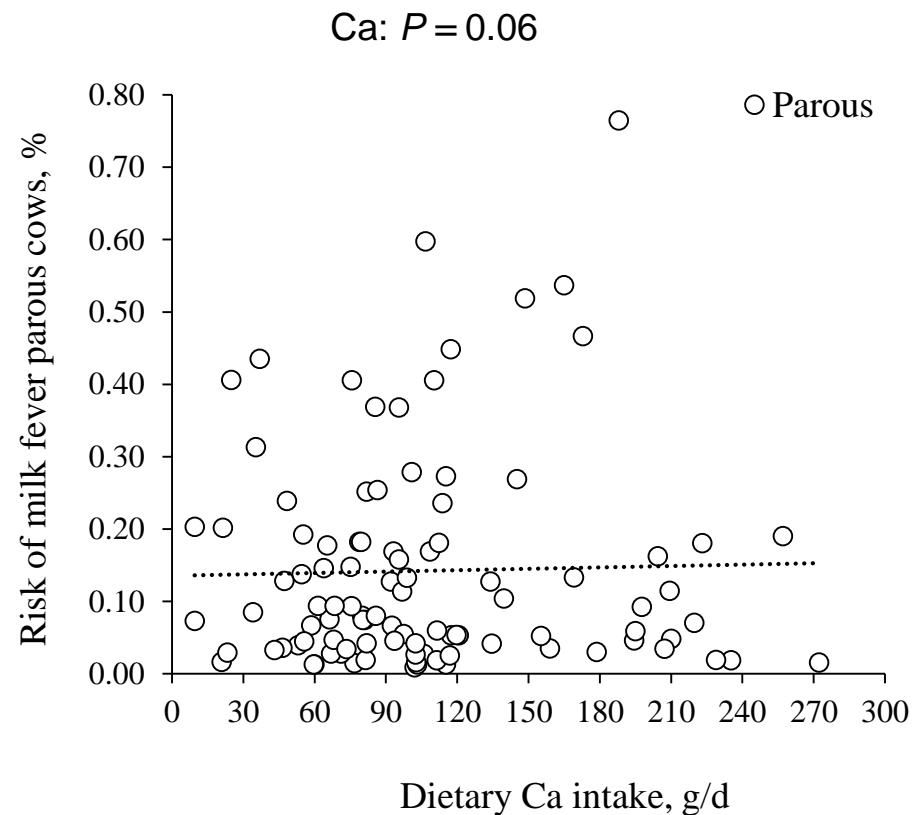
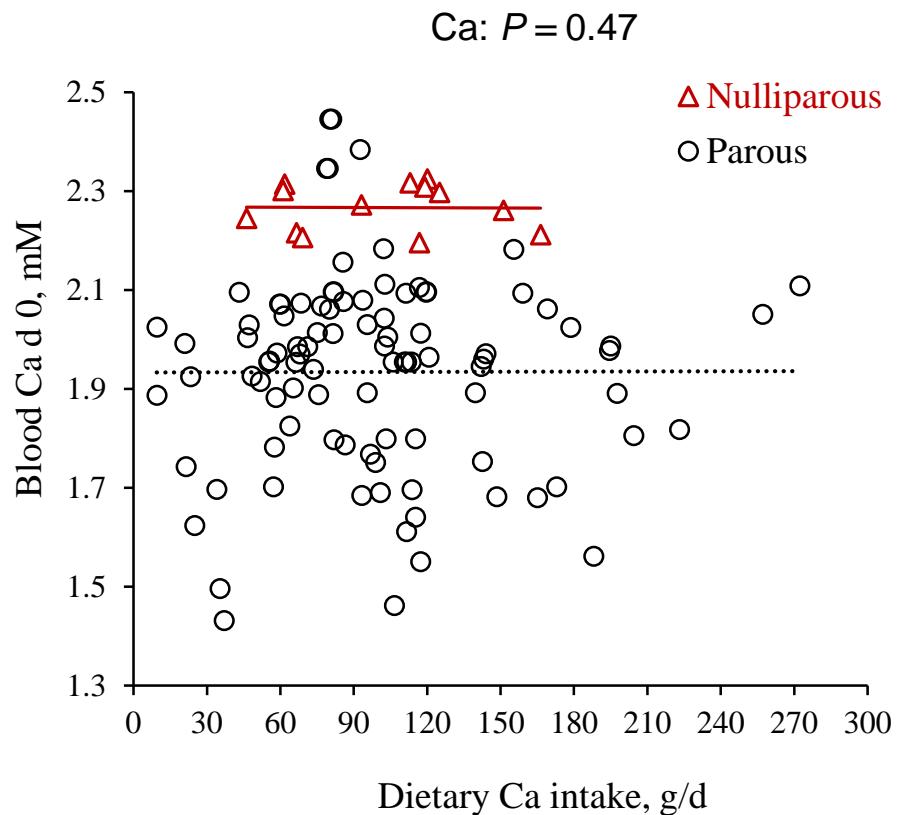
DCAD and DM Intake Postpartum



Effect of DCAD on Yields of Milk and FCM According to Parity



What About Intake of Ca Prepartum



Concentration of Ca in prepartum diets:

- No association with production
- No association with health (tended to increase milk fever)

Why Acidogenic Diets Depress DMI

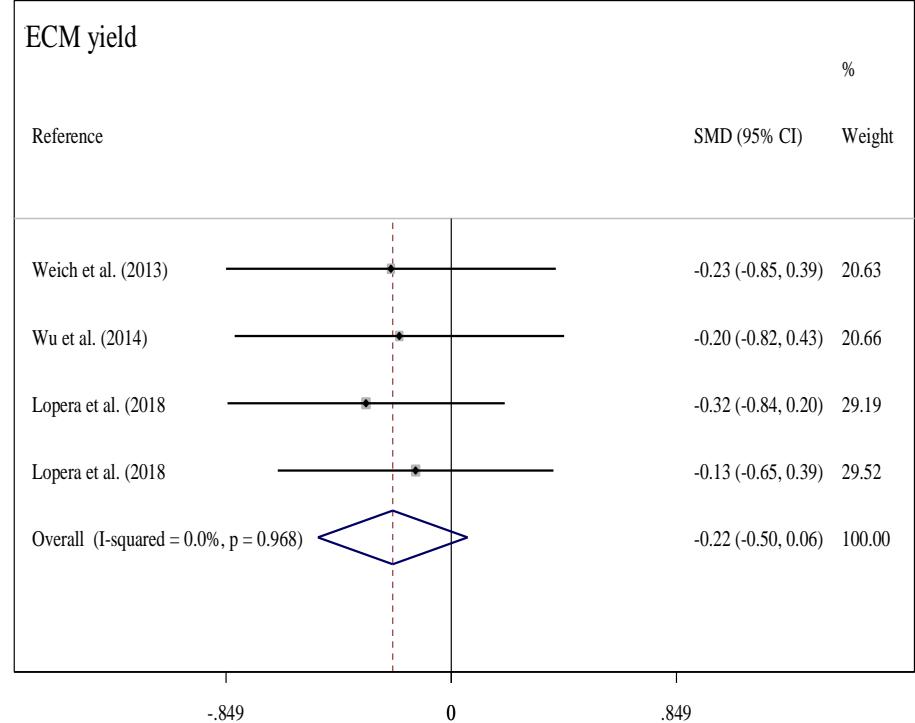
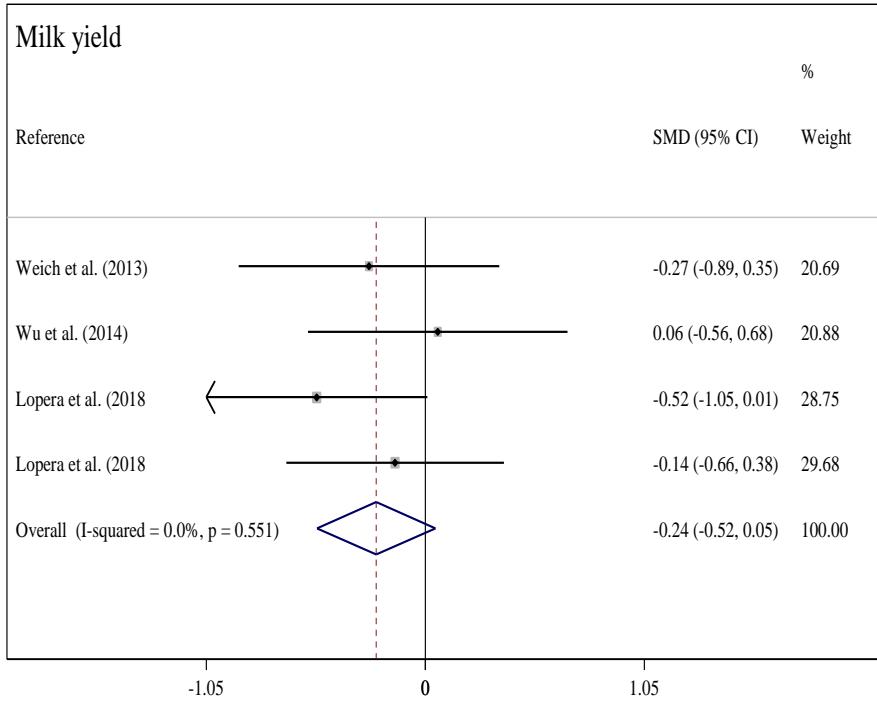
Ingredient, % DM	Treatment				
	TRT1	TRT2	TRT3	TRT4	TRT5
Corn silage	55.0	55.0	55.0	55.0	55.0
Bermuda hay	10.0	10.0	10.0	10.0	10.0
Concentrates	34.6	32.6	24.8	27.3	25.3
Acidogenic product	---	---	7.5	7.5	7.5
Sodium chloride	---	1.0	---	---	1.0
Potassium chloride	---	1.0	---	---	1.0
Na sesquicarbonate	---	---	1.5	---	0
Potassium carbonate	---	---	1.0	---	0
Magnesium oxide	0.4	0.4	0.2	0.2	0.2
K, %	1.42 ± 0.09	1.83 ± 0.04	1.71 ± 0.04	1.29 ± 0.05	1.78 ± 0.09
S, %	0.18 ± 0.03	0.18 ± 0.03	0.37 ± 0.04	0.39 ± 0.03	0.40 ± 0.04
Na, %	0.04 ± 0.02	0.42 ± 0.05	0.54 ± 0.10	0.13 ± 0.02	0.53 ± 0.05
Cl, %	0.26 ± 0.01	1.23 ± 0.13	0.89 ± 0.07	0.91 ± 0.05	2.03 ± 0.06
DCAD, ⁶ mEq/kg	196 ± 20	194 ± 45	192 ± 27	-114 ± 26	-113 ± 43

Depression in Intake Prepartum by Acidogenic Diets is Mediated by Metabolic Acidosis

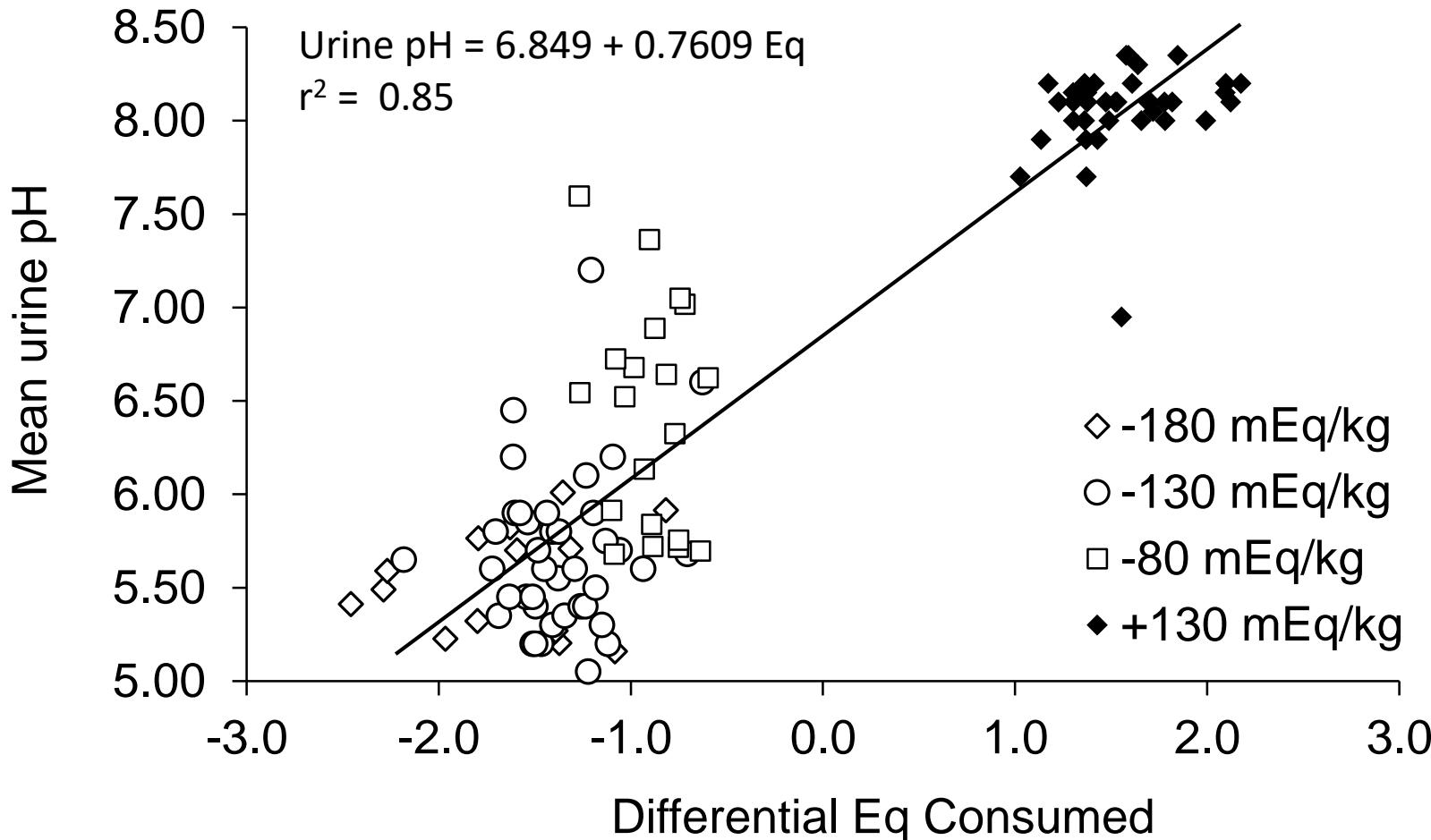
Item	Treatment					SE	P-value ¹			
	T1	T2	T3	T4	T5		AP	AB	ClAlk	ClAc
Blood pH	7.450	7.436	7.435	7.420	7.416	0.005	0.001	0.001	0.02	0.40
Base excess, mM	1.85	1.20	1.45	-0.20	-0.95	0.32	0.001	0.001	0.13	0.09
DMI, kg/d	10.3	10.2	10.2	9.7	9.5	0.2	0.02	0.003	0.60	0.30
DMI, % BW	1.76	1.75	1.74	1.68	1.64	0.03	0.03	0.003	0.63	0.14

¹ AP = contrast of effect of adding acidogenic product (T1 vs. T4); AB = contrast of acid-base status, alkalogenic vs. acidogenic diets (T2 + T3 vs. T4 + T5); ClAlk = contrast of adding Cl salts to an alkalogenic diet (T1 vs. T2); ClAc = contrast of adding Cl salts to an acidogenic diet (T4 vs. T5).

Feeding Acidogenic Diets During the Entire Dry Period



Urine pH is Affected by the Differential Eq Consumed, not just the Calculated DCAD



Conclusions

- ✓ Hypocalcemia is a gateway disease linked to increased risk of several other diseases in dairy cows
 - Best strategy is **prevention**
- ✓ Acidogenic diets have benefits beyond prevention of milk fever
 - ✓ Improved concentrations of Ca and P on the day of calving and Ca postpartum
 - ✓ Improved yields of milk, FCM, fat and protein in parous cows
 - ✓ Reduced incidence of milk fever, retained placenta, and metritis
- ✓ Little or no evidence that manipulating dietary Ca concentration or intake affects postpartum responses to acidogenic diets
- ✓ Limited evidence that increasing Mg to 0.3-0.4% of diet DM reduced milk fever and no evidence of a benefit to performance or risk of other diseases
- ✓ The ideal prepartum DCAD remains undetermined, but most likely around -100 mEq/kg



Thank you
Jepsantos@ufl.edu