Managing Calcium challenges at the onset of lactation

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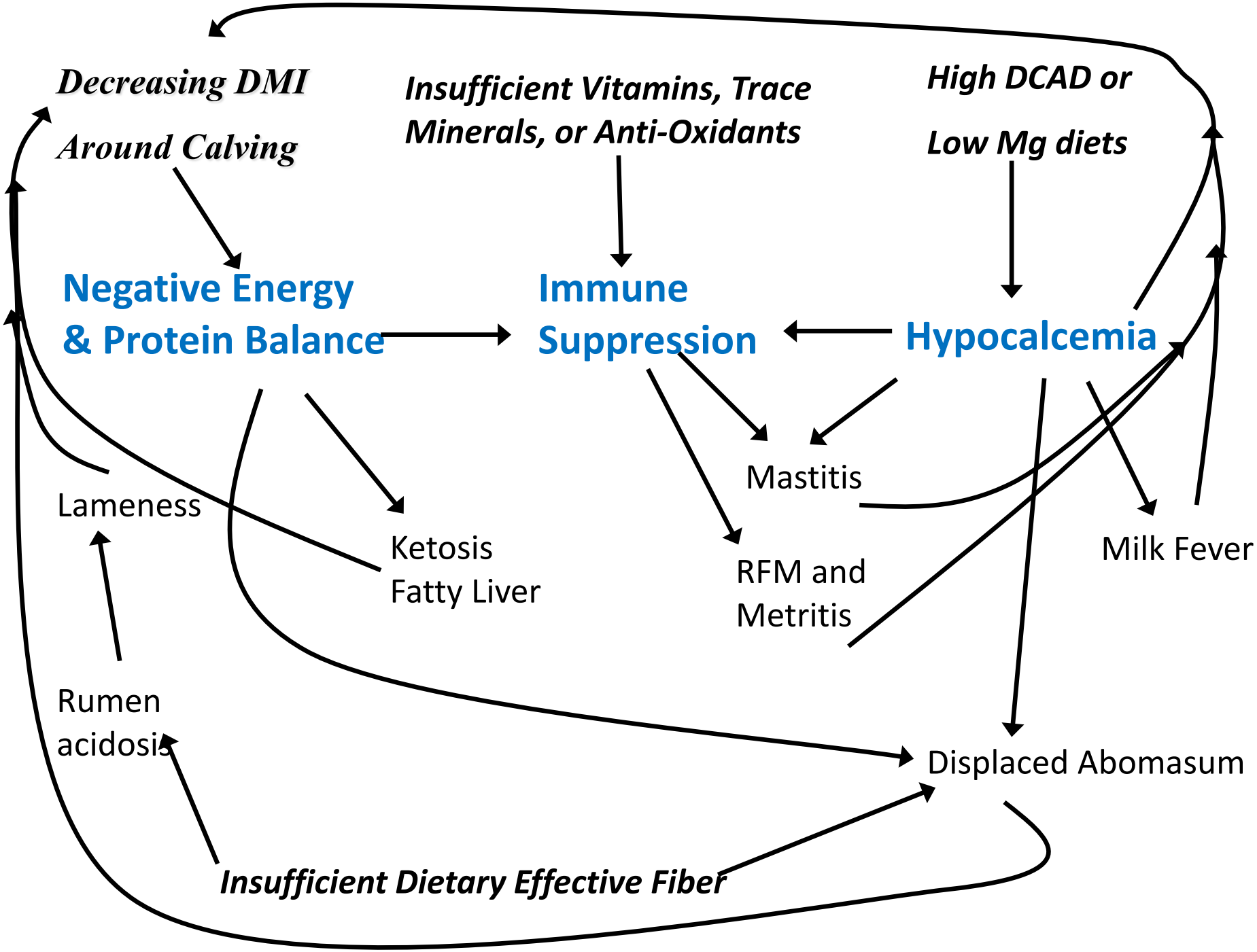
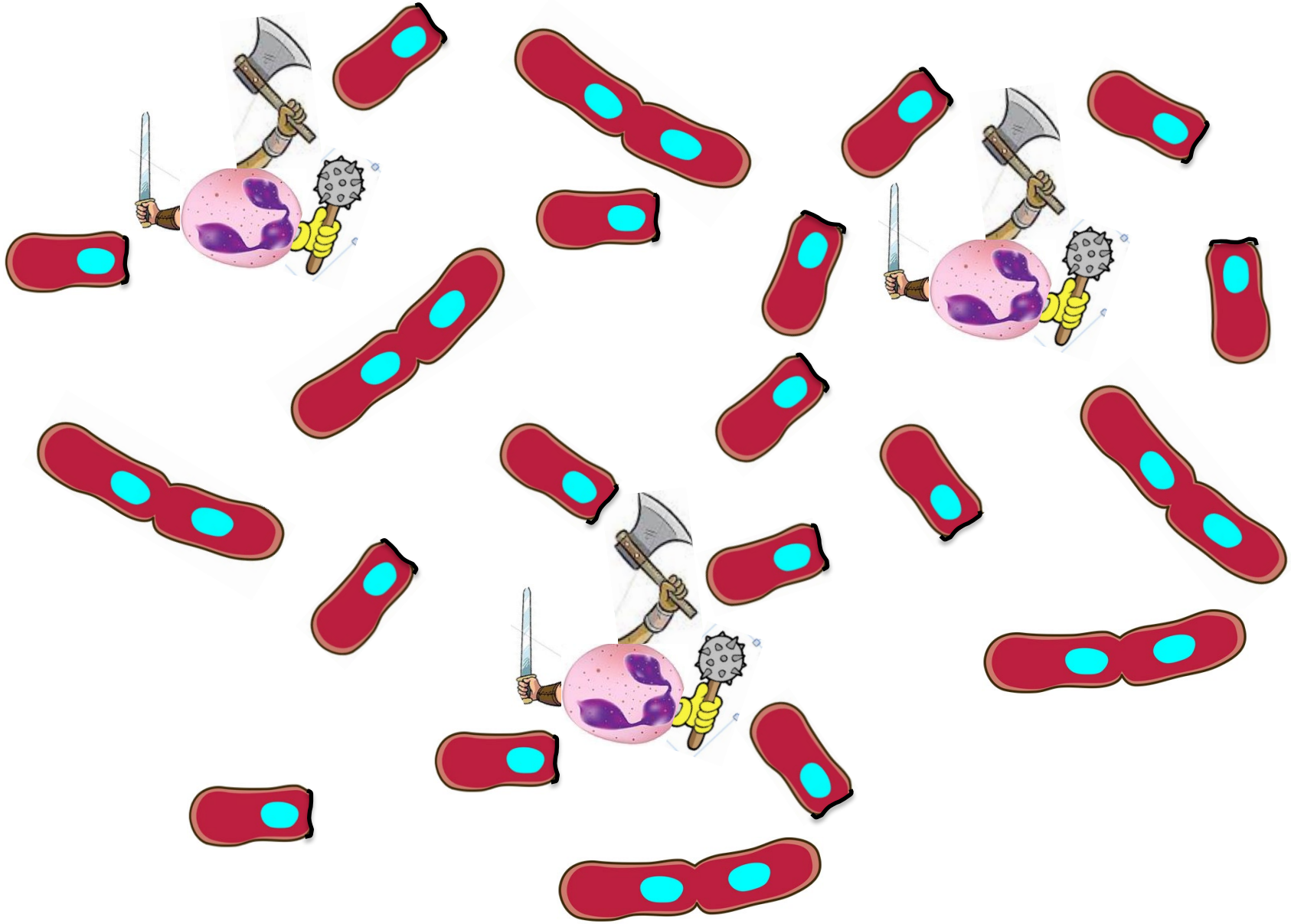
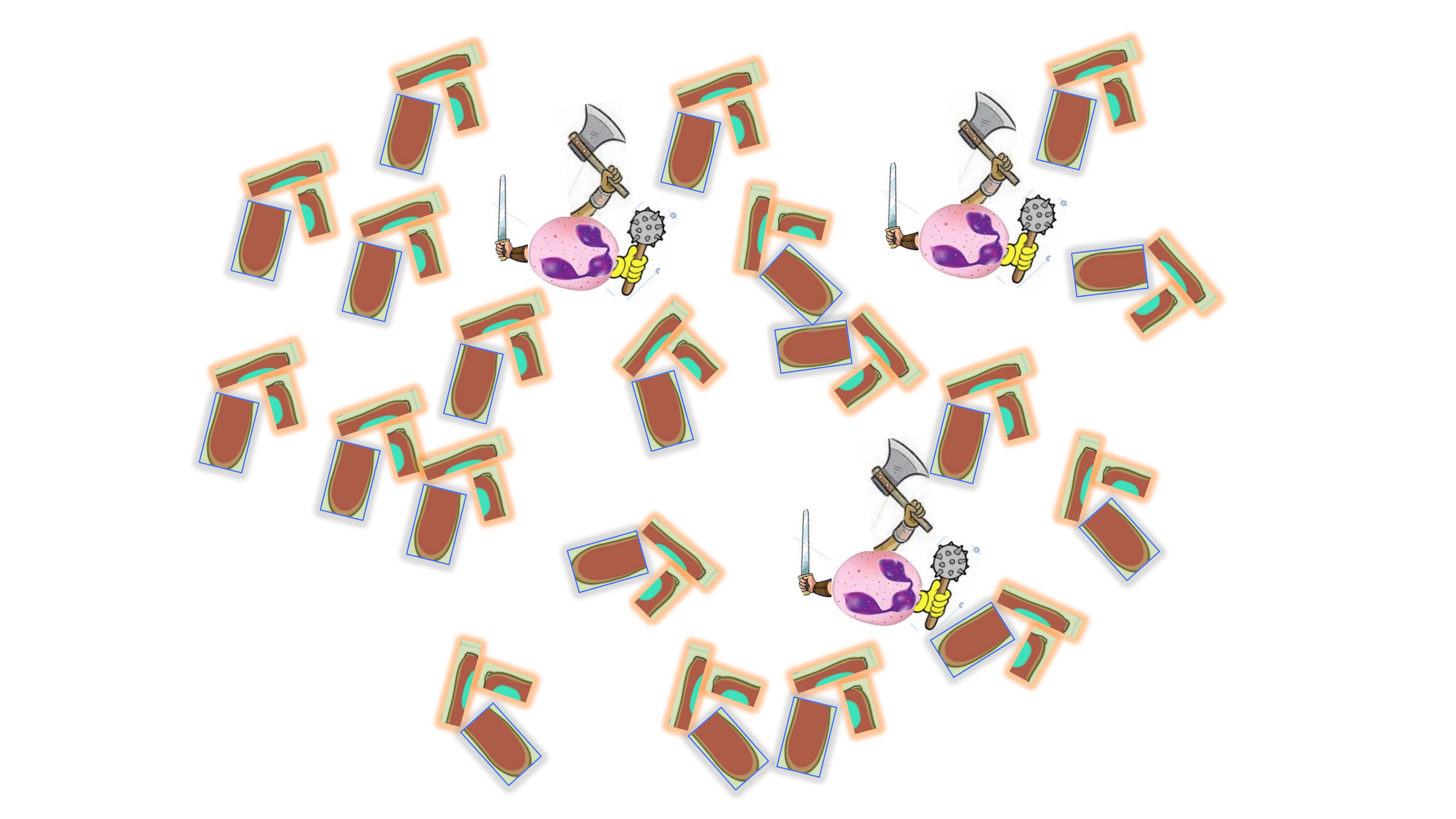

Decreasing DMI
Around Calving
Insufficient Vitamins, Trace Minerals, or Anti-Oxidants
High DCAD or
Low Mg diets
Negative Energy & Protein Balance
Immune Suppression
Hypocalcemia
Mastitis
Lameness
Ketosis
Fatty Liver
RFM and Metritis
Milk Fever
Rumen acidosis
Displaced Abomasum
Insufficient Dietary Effective Fiber

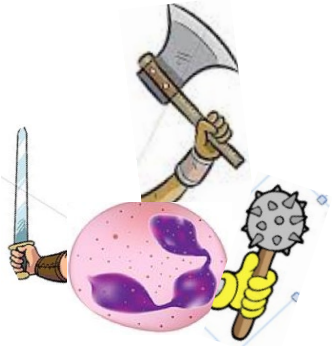
Bacterial Infection

STRONG IMMUNE SYSTEM



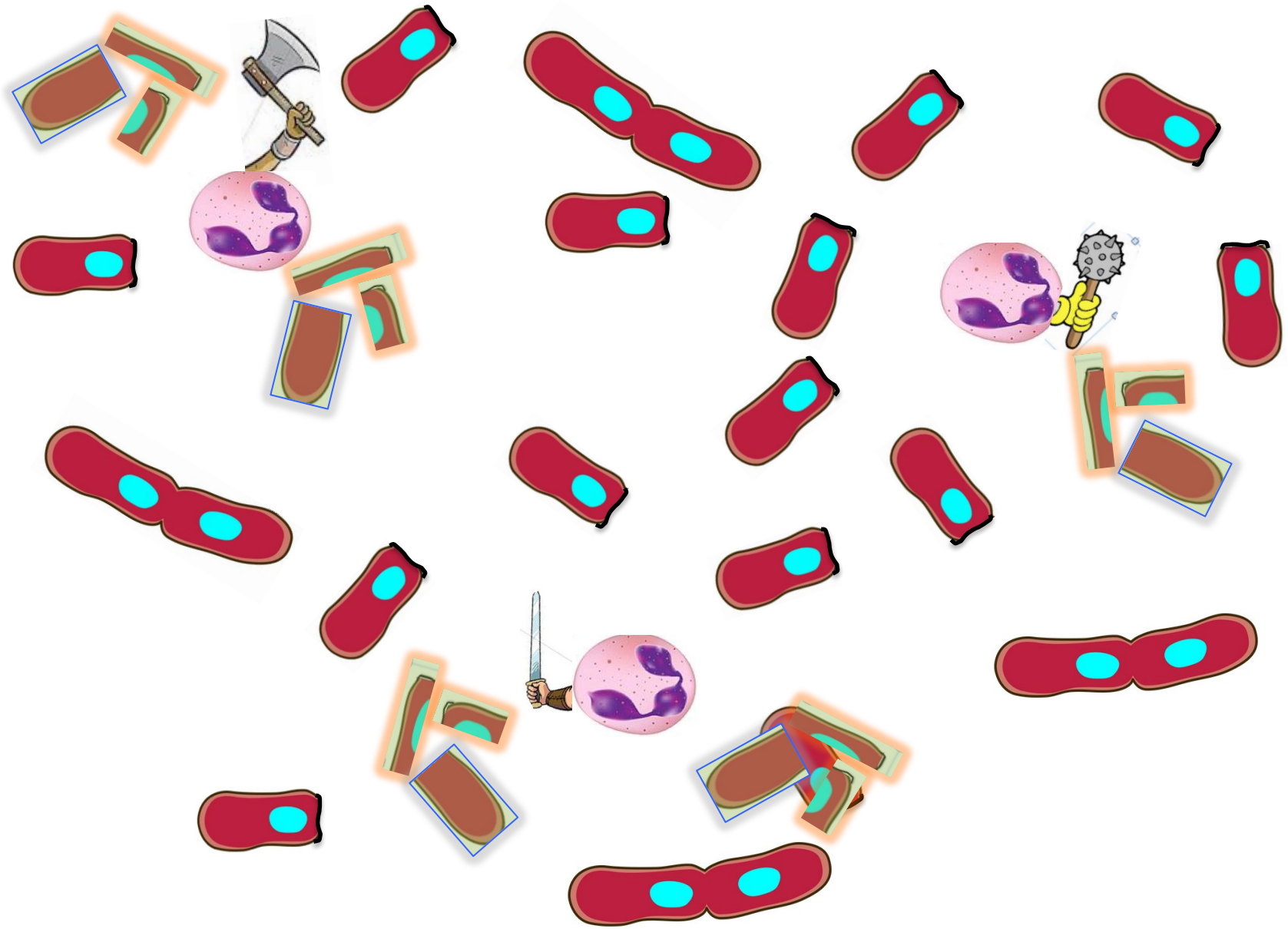


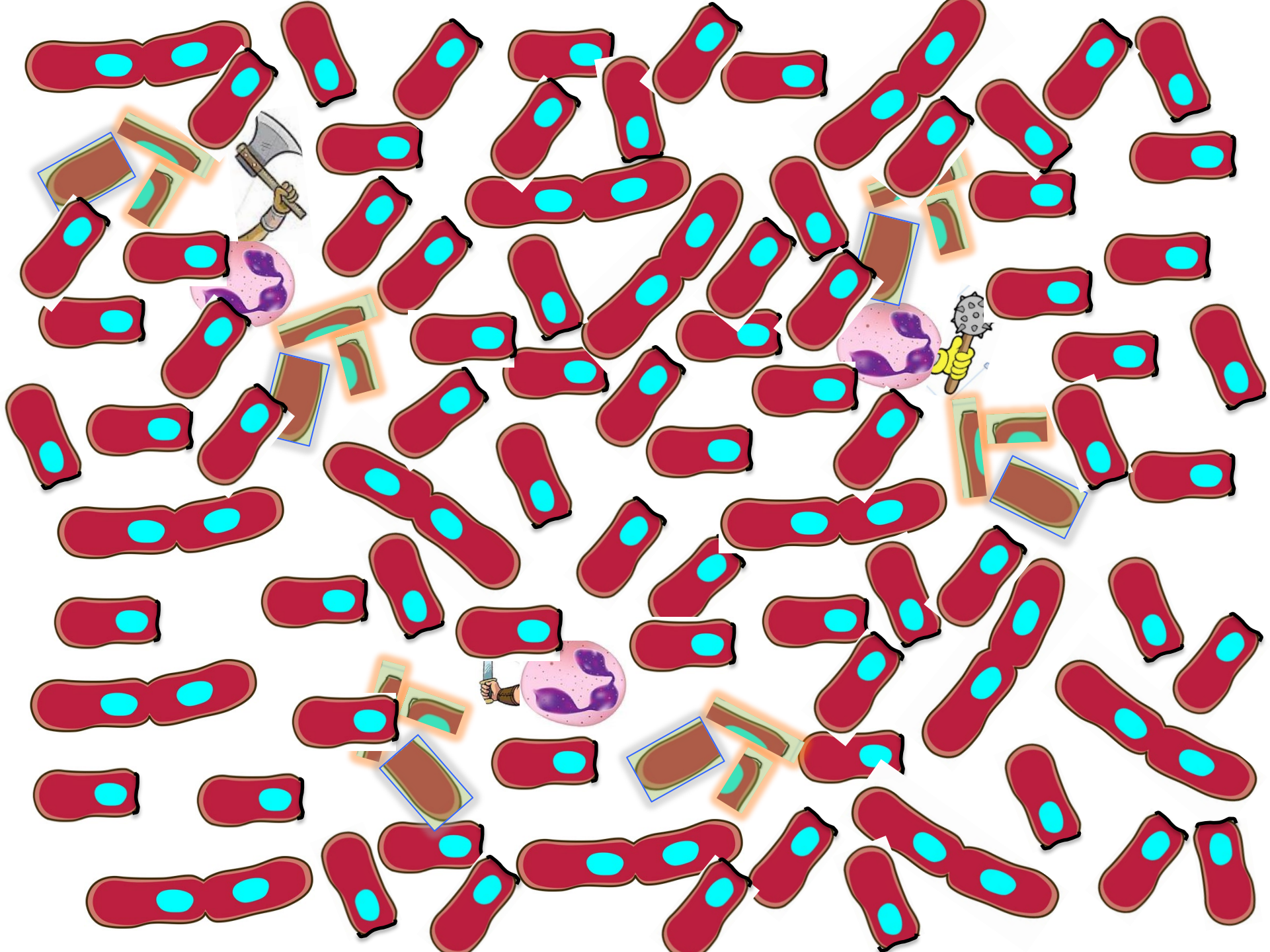
Infection Cleared



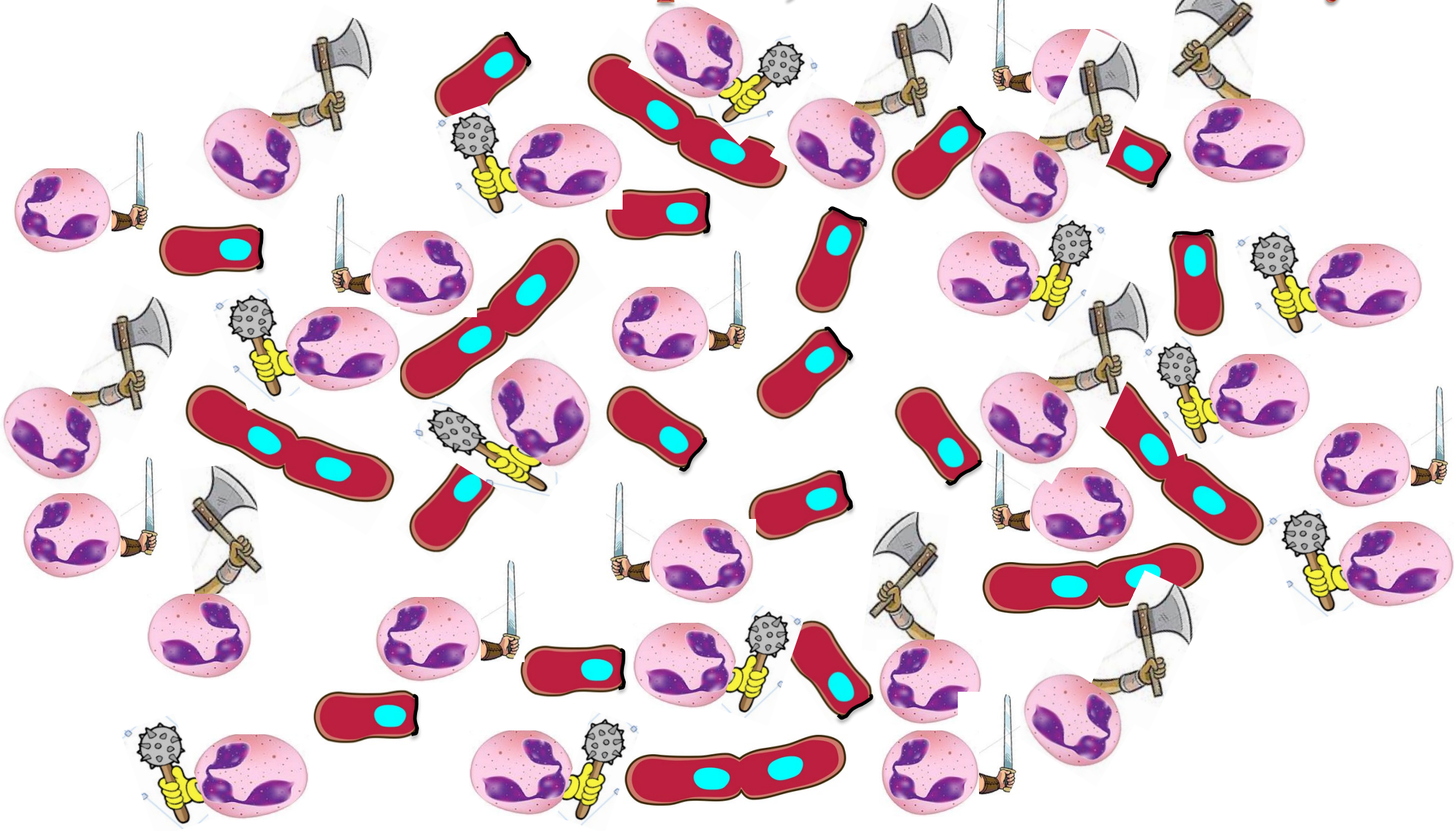
Bacterial Infection

Less Functional Neutrophils





Low function neutrophils, but 4-5 fold as many



Low function neutrophils, but 4-5 fold as many

Infection Cleared Eventually!?

BUT …. DURING CHRONIC INFLAMMATION THE COW EXPERIENCES

DECREASED DMI

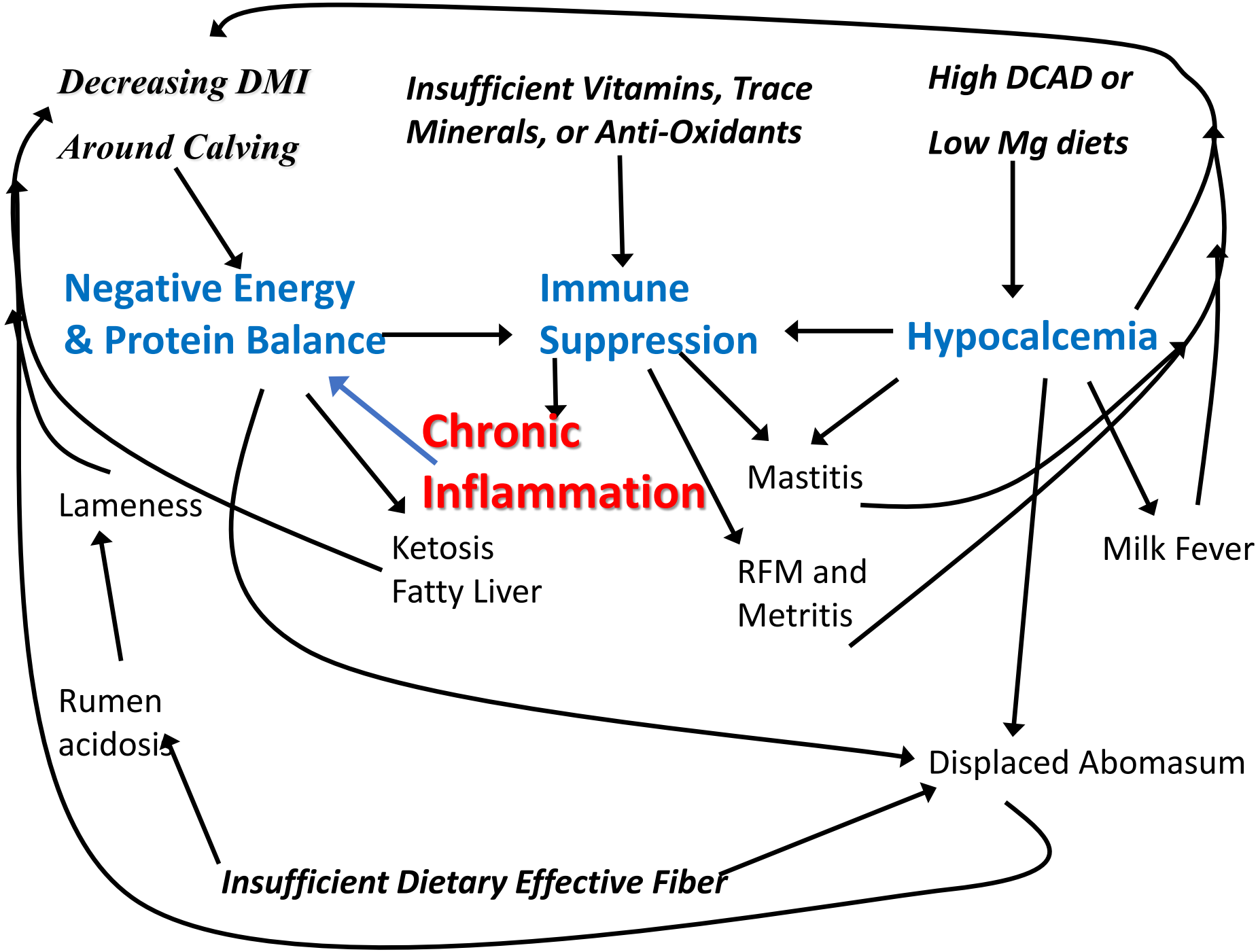
- MORE KETOSIS/ FATTY LIVER
- LESS RUMEN FILL= LESS ABOMASAL CONTRACTION
- LESS PROTEIN INTAKE → MORE MUSCLE LOSS

GREATER # BACTERIA TO KILL → MORE ENDOTOXINS

- AFFECTS LIVER FUNCTION
- INCREASED FATTY ACIDS RELEASE FROM ADIPOSE
- LOW GRADE HYPOCALCEMIA
- DECREASED INSULIN SENSITIVITY
- REDUCED BLOOD TO HOOF →MORE LAMENESS

TISSUE DAMAGE BY IMMUNE CELL RESPONSE

- GREATER DAYS OPEN
- LESS MILK PRODUCTION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Insufficient Dietary Effective Fiber

Normal Blood Calcium concentration = 9-10 mg / dl (2.25-2.5 mM).

Clinical Hypocalcemia = Milk Fever – Blood Ca < 4.5 mg/dl (1.1 mM) (1-5% of cows)

Cow unable to rise to feet, No rumen motility, Severe drop in Dry matter intake. High degree of immune suppression. MUCH LESS MILK & SHORTER LIFESPAN

- more retained placenta, metritis and repro problems
- more ketosis
- more displaced abomasum
- more mastitis

Subclinical – Blood Ca < 8 mg/dl (2.0 mM) in first few days after calving. (25-65% of cows).

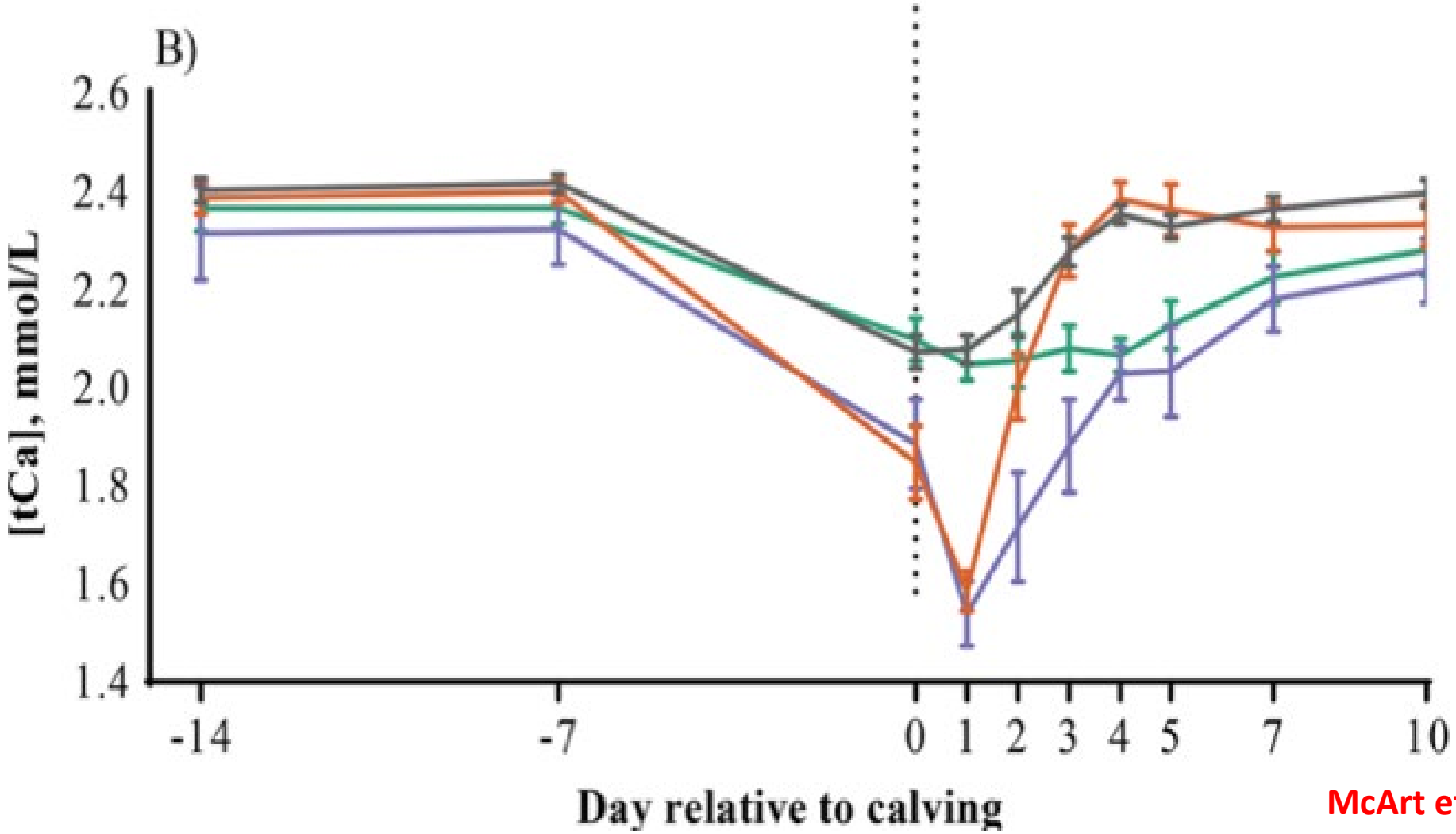
Rumen motility and dry matter intake depressed. Immune suppression. Increases risk of secondary disease, but not as much as clinical milk fever. LESS MILK!

Some cows do not develop any hypocalcemia (black).

Transient hypocalcemia (red) associated with higher milk production.

Persistent hypocalcemia (purple) associated with higher cull rate.

A few cows develop hypocalcemia after day 2 of lactation (green).



McArt et al., 2020 J D S

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TISSUE DAMAGE

- GREATER DAYS OPEN
- LESS MILK PRODUCTION

Hypocalcemia can Contribute to Chronic Inflammation

Cows with hypocalcemia have low Ca++ in neutrophils and reduced neutrophil migration, adhesion, and phagocytosis

Kimura et al., 2006; Zhang et al., 2019

The relative risk of developing metritis decreased by 22% for every 1mg/dL increase in serum Ca.

Martinez et al., 2012

Inflammation Can Cause Hypocalcemia

Mastitis and metritis cows often show concurrent hypocalcemia.

tCa ~ 6-8 mg/dl. Wenz et al., JAVMA 2001; Waldron et al., 2003.

Acute Infections - endotoxins

Table 2. Hematological values and number of somatic cells in milk of peracute coliform mastitic cows (day 0 to day 3) and healthy cows

Parameters	Healthy cows (8)	Day0 (11)	Day 2 (11)	Day 3 (11)
Hematocrit values (%)	28.7 ± 1.4	32.7 ± 3.9	30.1 ± 4.6	29.4 ± 5.2
Leukocyte counts (/μl)	13,250 ± 5,742.8	6,136.4 ± 4,405.9[a)]	12,600 ± 9,948.3	15,845.4 ± 8,856.1[a)]
Platelet counts ($\times 10^4/\mu l$)	49.3 ± 3.5	39.0 ± 17.7	38.2 ± 16.6	39.9 ± 16.7
Total protein (g/dl)	7.35 ± 0.50	5.63 ± 1.87	5.91 ± 1.39	6.34 ± 1.77
Albumin (g/dl)	3.53 ± 0.13	2.71 ± 0.85	2.82 ± 0.67	2.96 ± 0.84
A/G (%)	0.90 ± 0.18	0.96 ± 0.20	0.94 ± 0.21	0.89 ± 0.17
Blood urea nitrogen (mg/dl)	10.8 ± 4.2[b)]	17.3 ± 4.3[b,c)]	14.1 ± 5.2	11.3 ± 2.1[c)]
Total cholesterol (mg/dl)	212.75 ± 53.72	139.91 ± 57.56	149.72 ± 72.57	151.36 ± 57.05
Total calcium (mmol/l)	2.48 ± 0.34[d)]	1.52 ± 0.55[d)]	1.87 ± 0.68	1.94 ± 0.59
Ionized calcium (mmol/l)	1.1 ± 0.1	0.98 ± 0.22	1.07 ± 0.16	1.07 ± 0.16
Inorganic phosphorus (mg/dl)	5.60 ± 2.05	3.47 ± 1.53	3.83 ± 1.56	4.52 ± 1.40
Magnesium (mg/dl)	2.16 ± 0.37	1.78 ± 0.56	1.71 ± 0.36	1.88 ± 0.56
Number of somatic cells in milk ($\times 10^3$/ml)	49.3 ± 3.5[e,f,g)]	25,638.1 ± 32,127.2[e)]	25,541.4 ± 35,022.5[f)]	10,270.3 ± 18,418.7[g)]

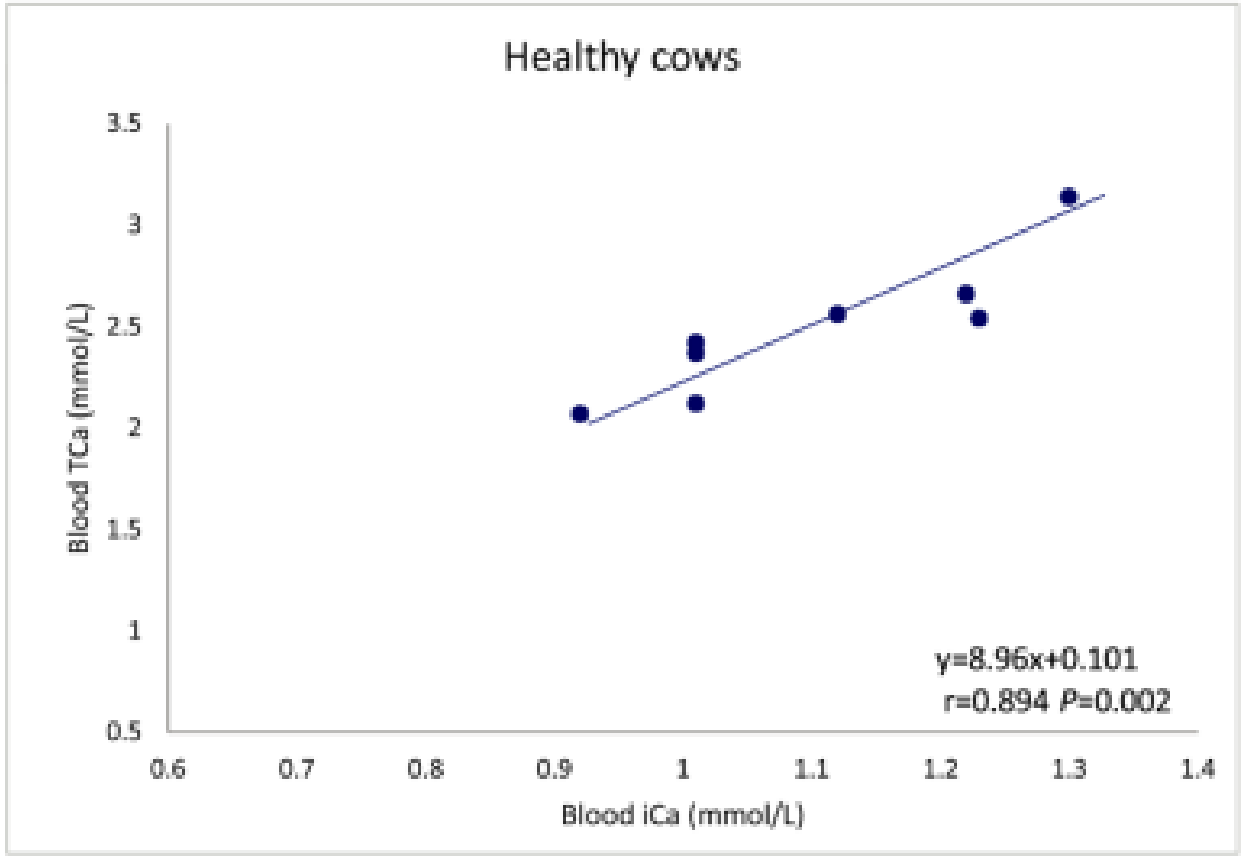
Each value represents the mean ± SD of the number of experiments (n). Values with the same letters are significantly different (e, f, and g are siginificant as $P<0.01$ and a, b, c, d are at $P<0.05$).

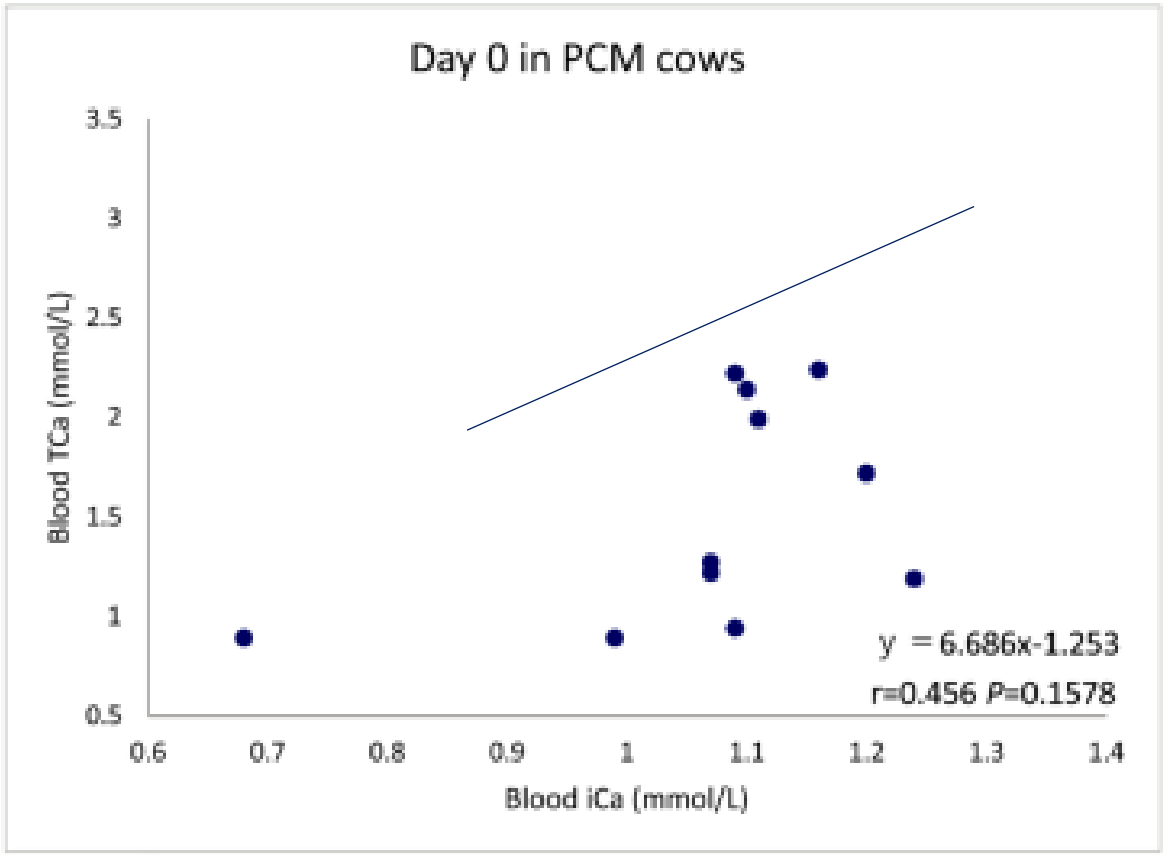
39% decrease in total Ca and 23% decrease in albumin

Hisaeda et al., JVMS 2019

Peracute mastitis causes hypocalcemia and disconnect between iCa and tCa

- disconnect associated with hypothermia, blood coagulation system activation, and dehydration, *and low blood albumin*





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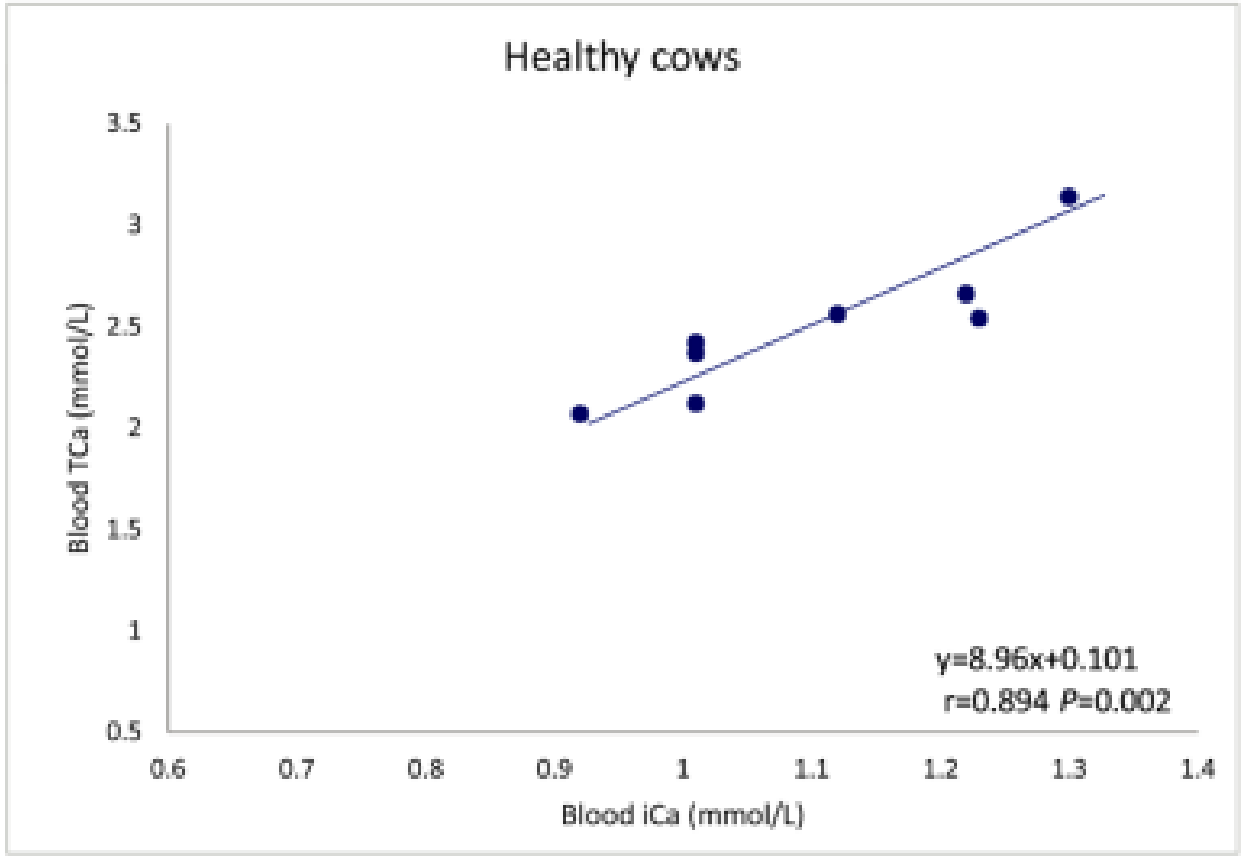
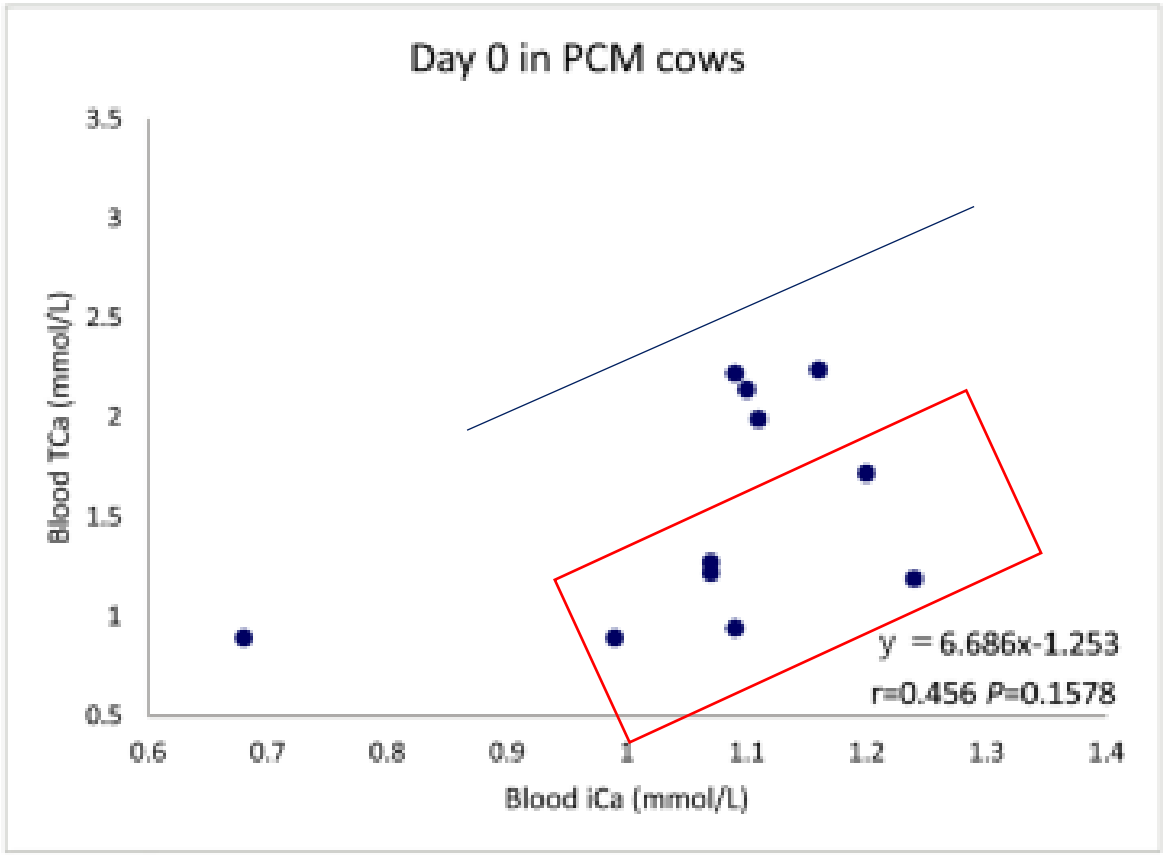




Hisaeda et al., JVMS 2019

Acute Infections – endotoxins

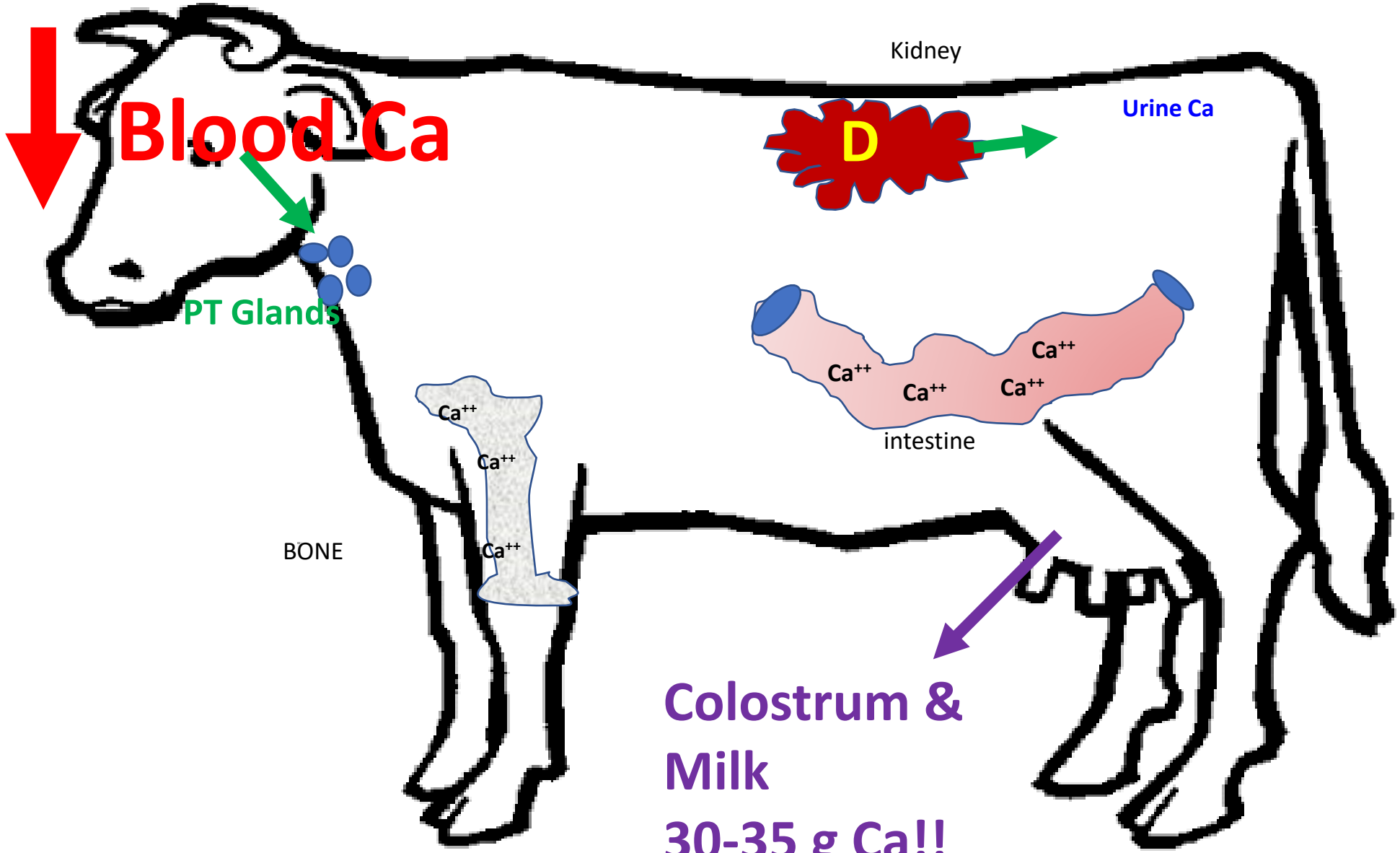
THIS IS NOT MILK FEVER!!

TREATING THESE COWS WITH IV CALCIUM MAKES THINGS WORSE!!!!

Cardiac arrest

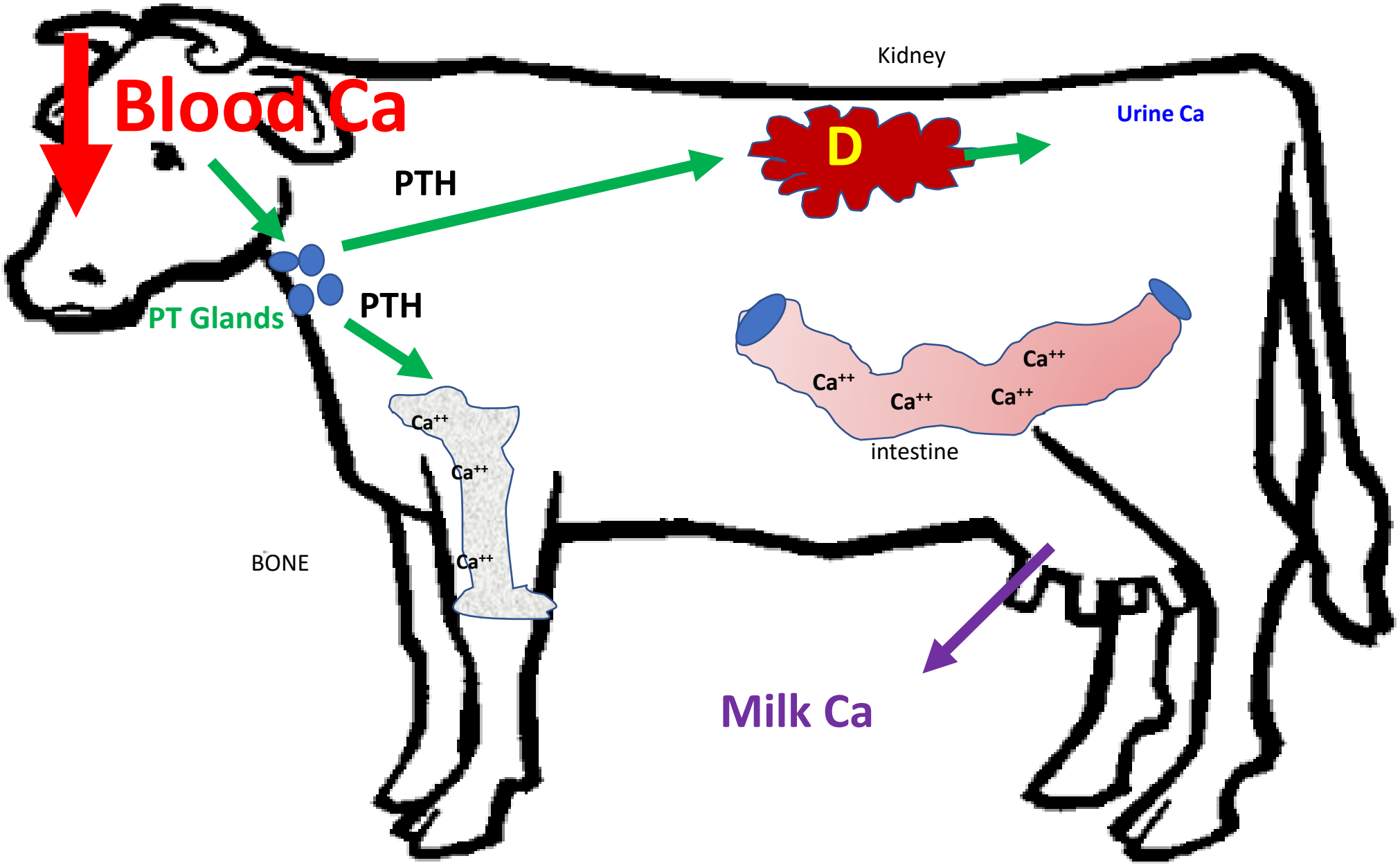
Renal impairment

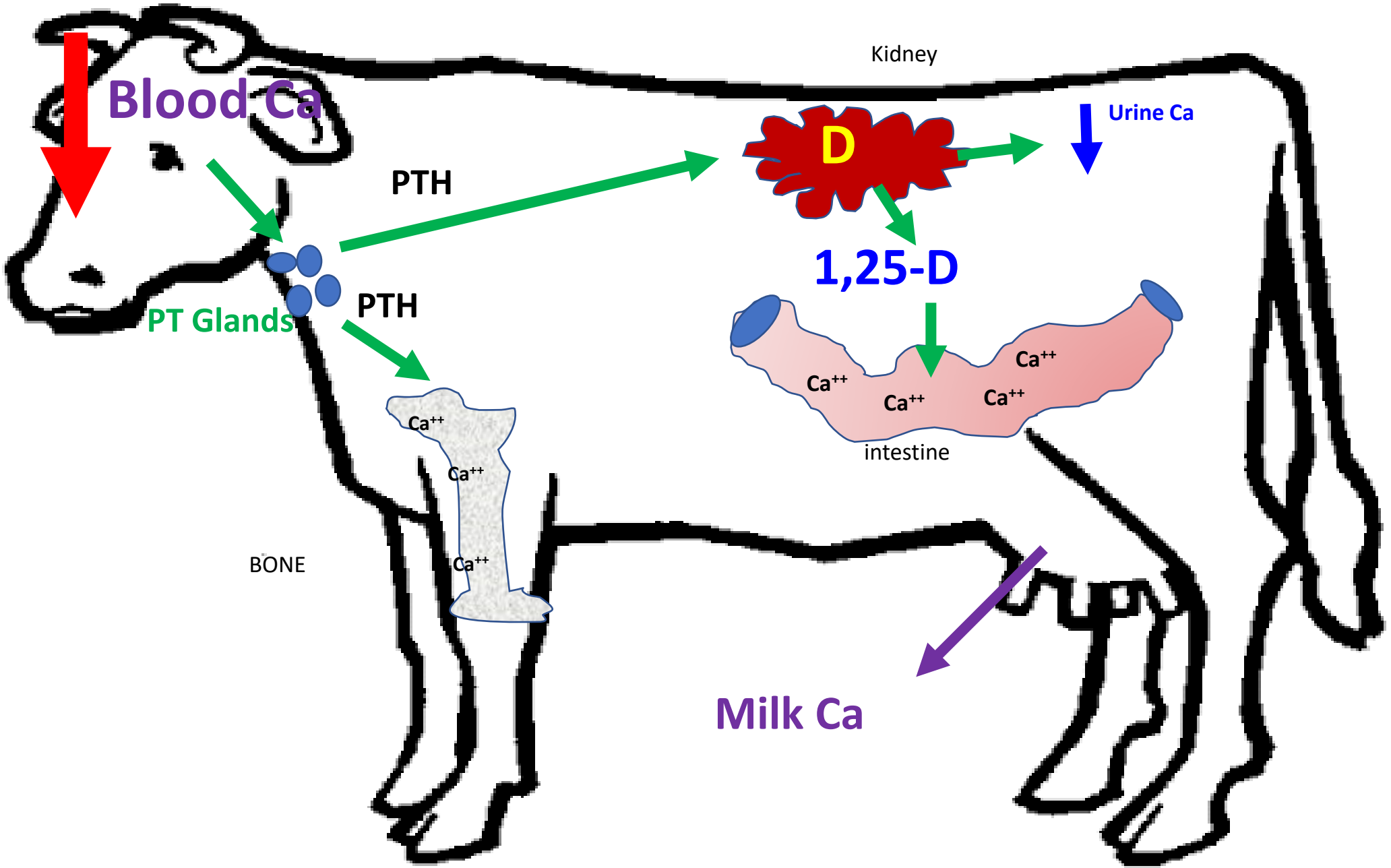
Why does blood Ca fall in almost every cow??



Why don’t all cows get milk fever????

Calcium Homeostasis!


Blood Ca
Kidney
Urine Ca
D
PTH
PTH
PT Glands
Ca++
Ca++
Ca++
Ca++
Ca++
Ca++
intestine
BONE
Milk Ca


Blood Ca
PTH
PT Glands
PTH
Kidney
D
Urine Ca
1,25-D
Ca++
Ca++
Ca++
Ca++
intestine
Ca++
Ca++
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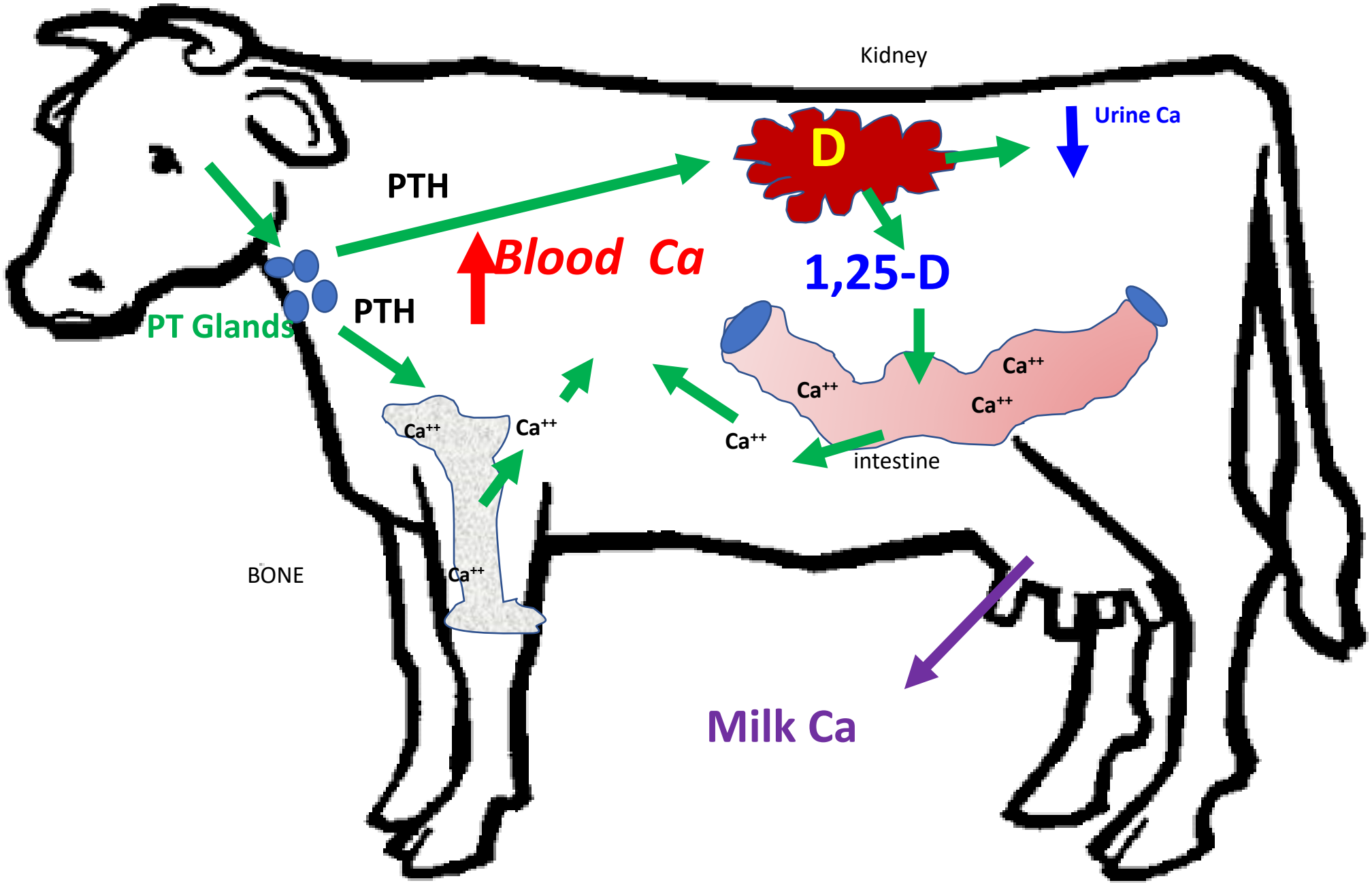
BONE
Milk Ca


Kidney
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Ca++
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Ca++
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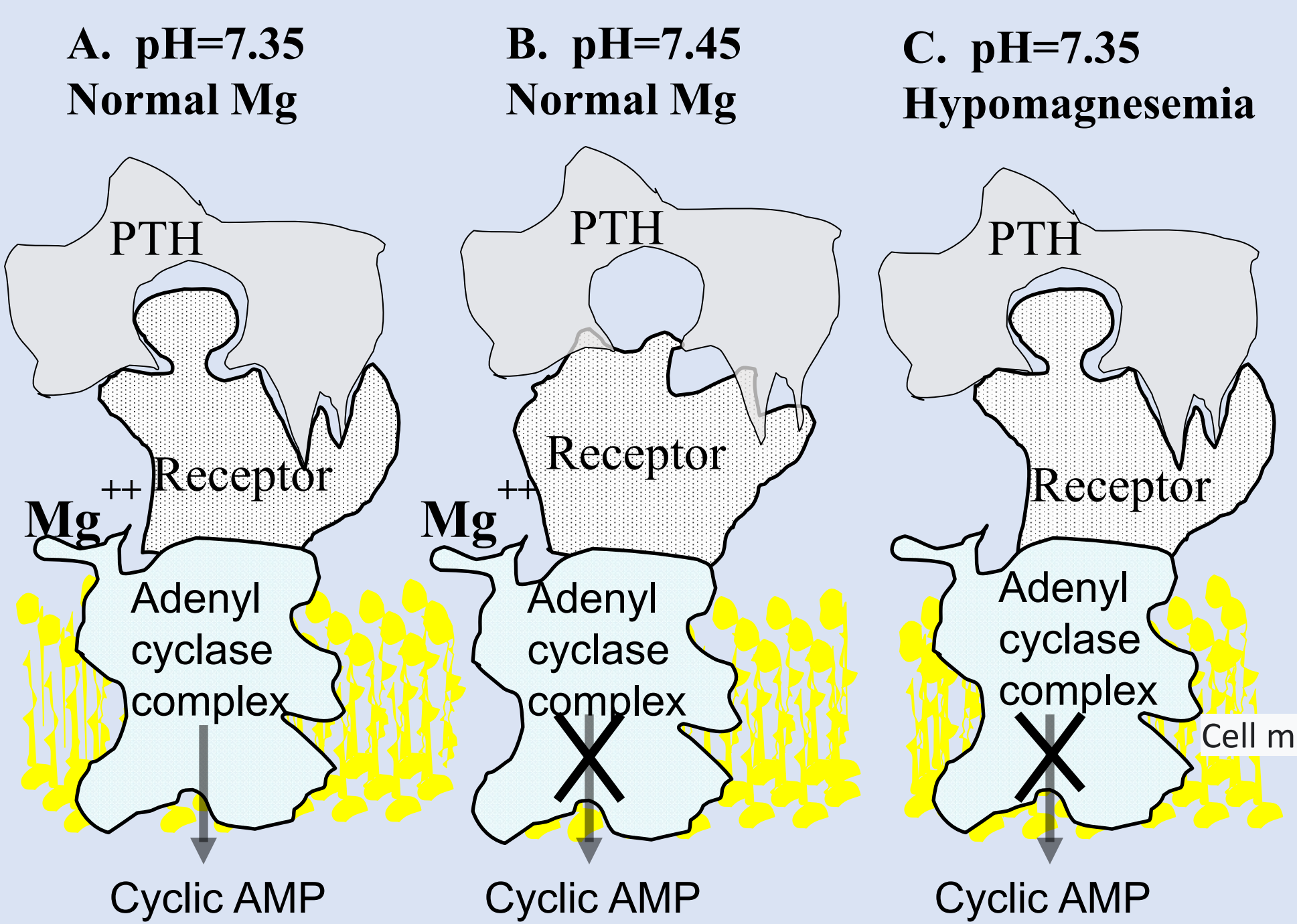
Ca++
intestine
BONE
Milk Ca

Why doesn’t Ca Homeostasis work in all cows???

Aged cows lose vitamin D receptors in intestine

Aged cows have fewer sites of active bone resorption (fewer osteoclasts) capable of responding to PTH rapidly

BLOOD pH AFFECTS BONE AND KIDNEY RESPONSIVENESS TO PTH!


A. pH=7.35
Normal Mg
B. pH=7.45
Normal Mg
C. pH=7.35
Hypomagnesemia
PTH
Receptor
++
Mg
Adenyl
cyclase
complex
Cyclic AMP
PTH
Receptor
++
Mg
Adenyl
cyclase
complex
Cyclic AMP
PTH
Receptor
Adenyl
cyclase
complex
Cyclic AMP
Cell membrane

Blood pH is dependent on Diet Cation –Anion Difference

DCAD 1 = (mEq Na^+ + mEq K^+)- (mEq Cl^- + mEq SO^{-2}_4)

Cations (+) ***absorbed*** from forages and diet cause the blood and urine of the cow to become alkaline

Anions (-) ***absorbed*** from forages and diet cause the blood and urine of the cow to become acidic

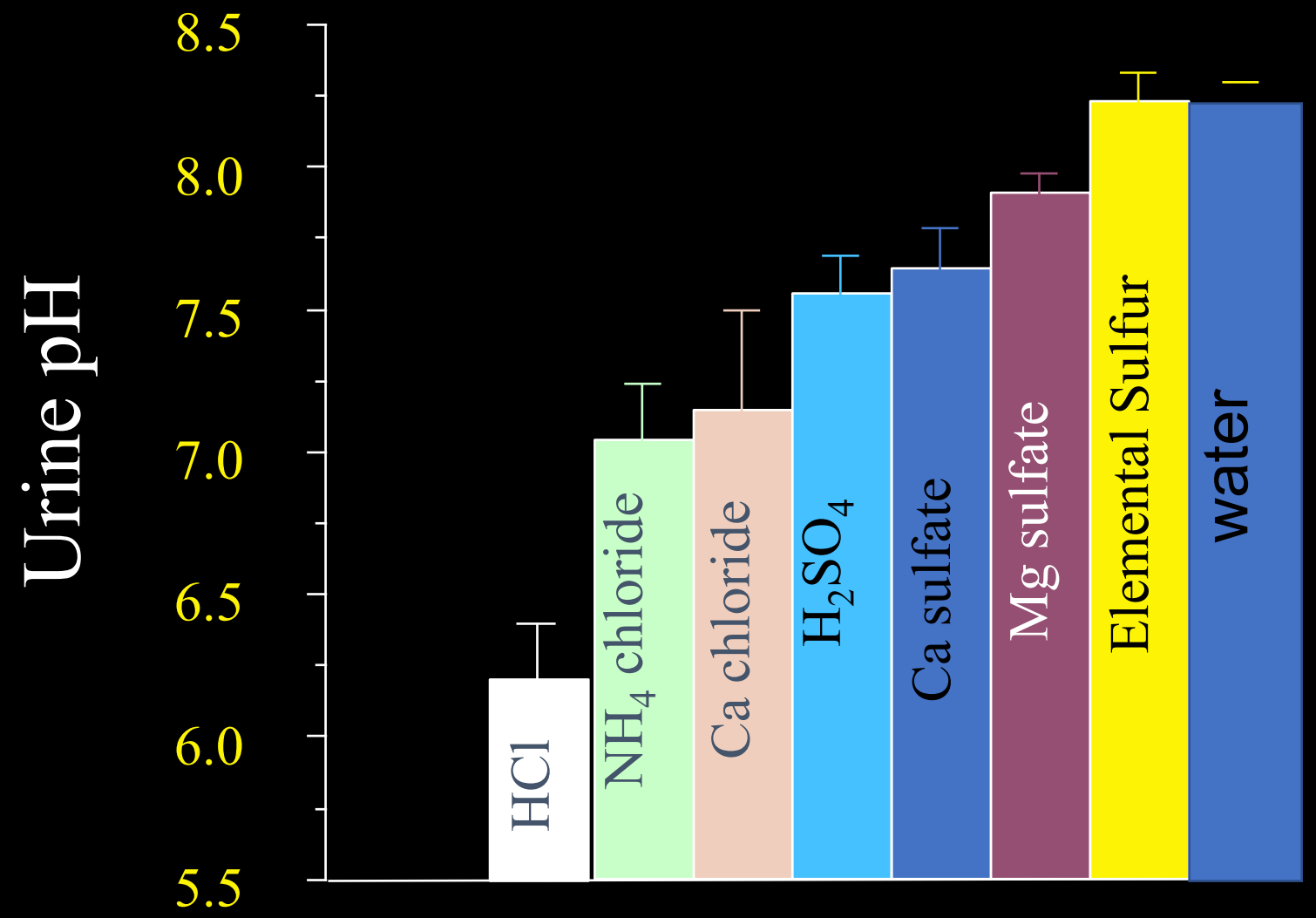
High DCAD diets, where K and Na are in much greater concentration than Cl or SO_4 , cause Alkalosis & milk fever

Milk Fever & Hypocalcemia Prevention

1. Avoid very high potassium forages for close-up cows; practiced by most dairies in US.
2. **Add anions (Cl or Sulfate) to diet to reduce blood and urine pH and improve tissue ability to respond to PTH!.**

Choosing the right anion sources

2 Eq of each anion source fed



Sulfate anion is only 60% as acidifying as chloride anions

Goff, et al 2006

DCAD Equations

DCAD 1 = (mEq Na^{+} + mEq K^{+}) - (mEq Cl^{-} + mEq SO^{-2}_{4})

DCAD 2 = (mEq Na^{+} + mEq K^{+}) - (mEq Cl^{-} + 0.6 mEq SO^{-2}_{4})

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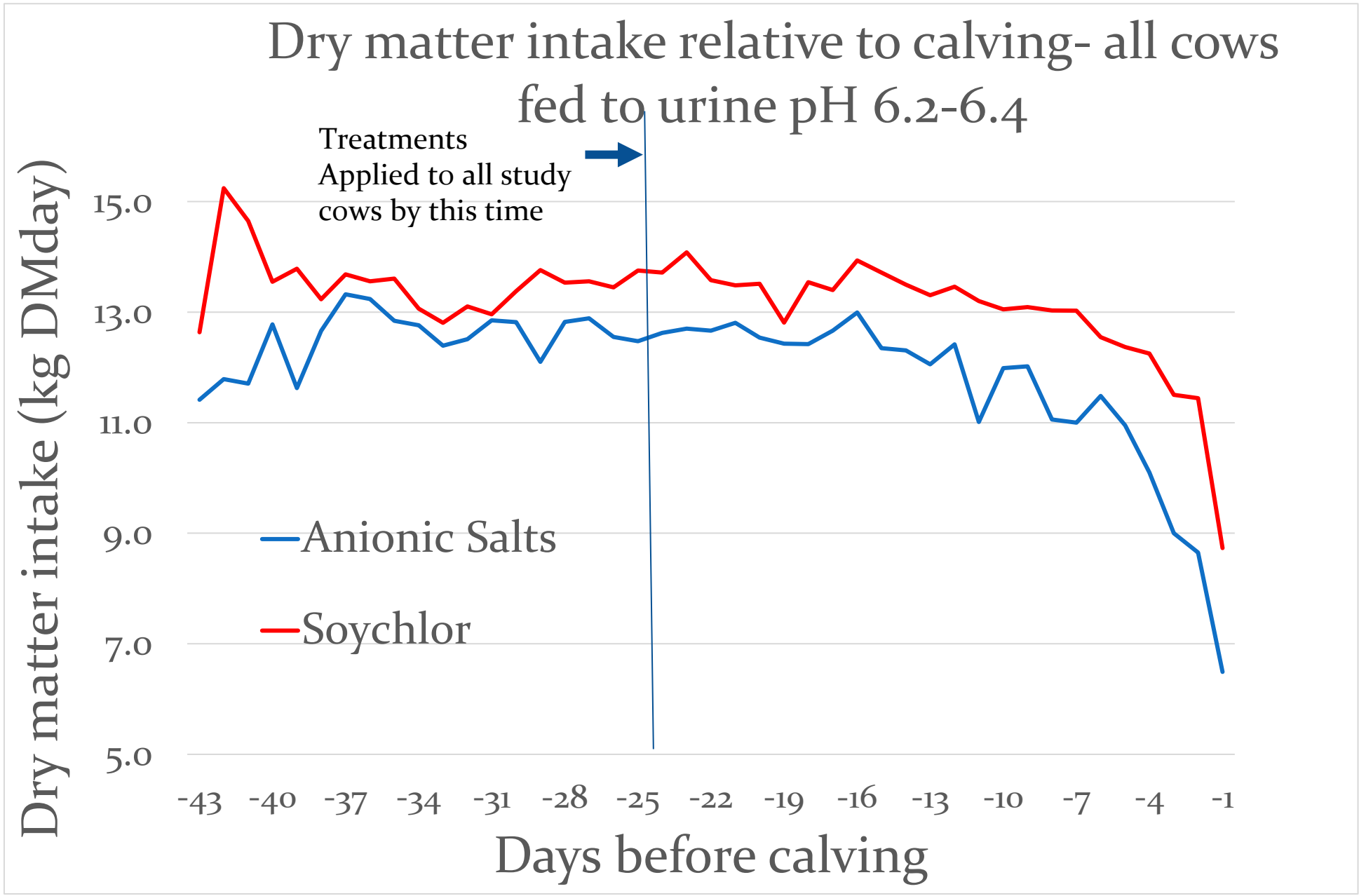
Choosing the right anion sources

Palatability Issues

-traditional salts had palatability problems



Strydom & Swiegart, 2016 ADSA

Is Dry Matter Intake Important???

Every 1-kg decrease in average DMI during the last week before calving increased the risk of subclinical ketosis by 2.2 times (Goldhawk et al. 2009).

Cows with a lower DMI prepartum are 3 times more likely to be diagnosed with metritis (Huzzey et al., 2007).

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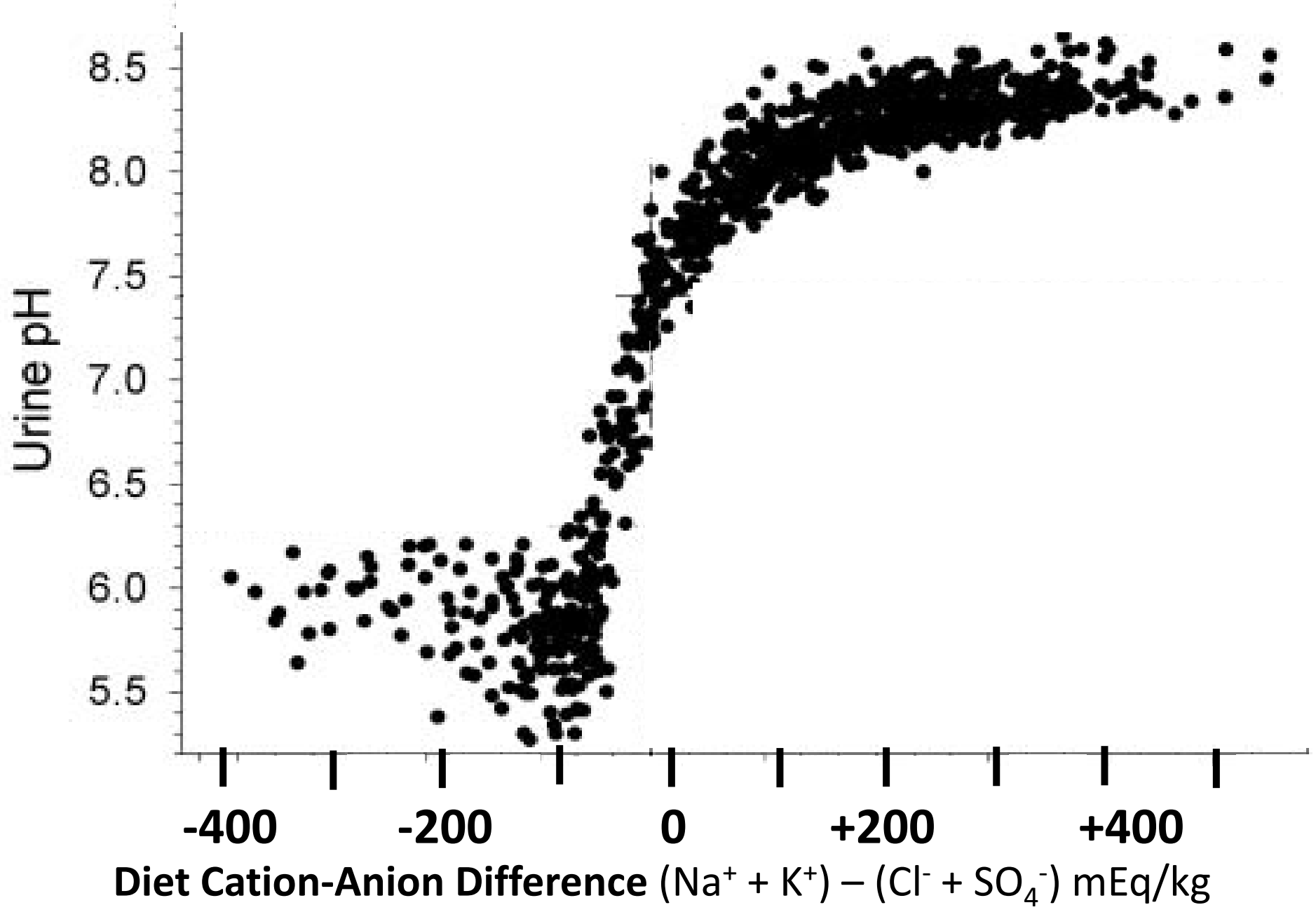
   Choosing the right anion sources

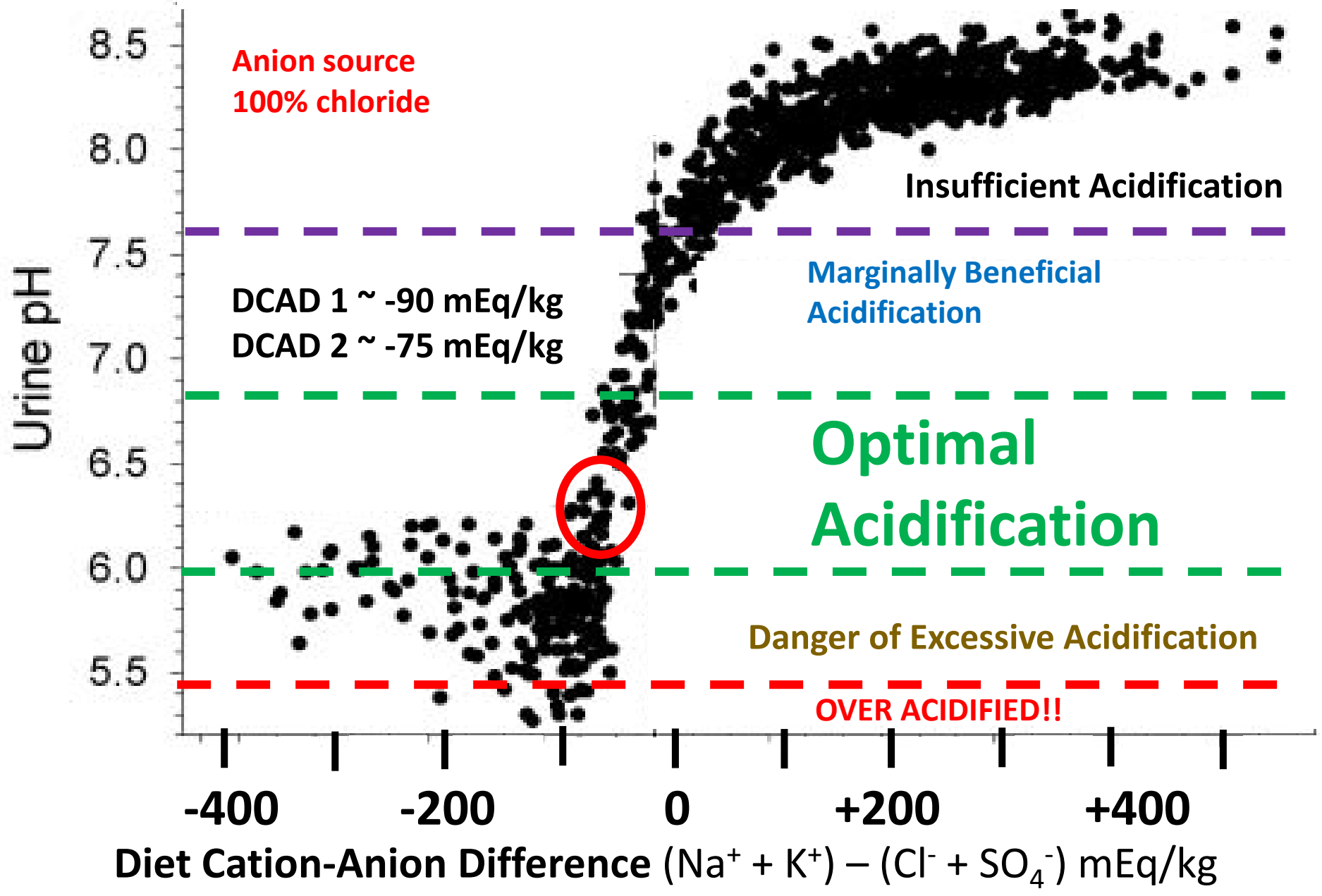
   Palatability Issues

Over and under acidification

-blood pH and urine pH decrease when DCAD decreases



Adapted from Constable et al., 2017; Spanghero, 2004; and Charbonneau et al., 2006



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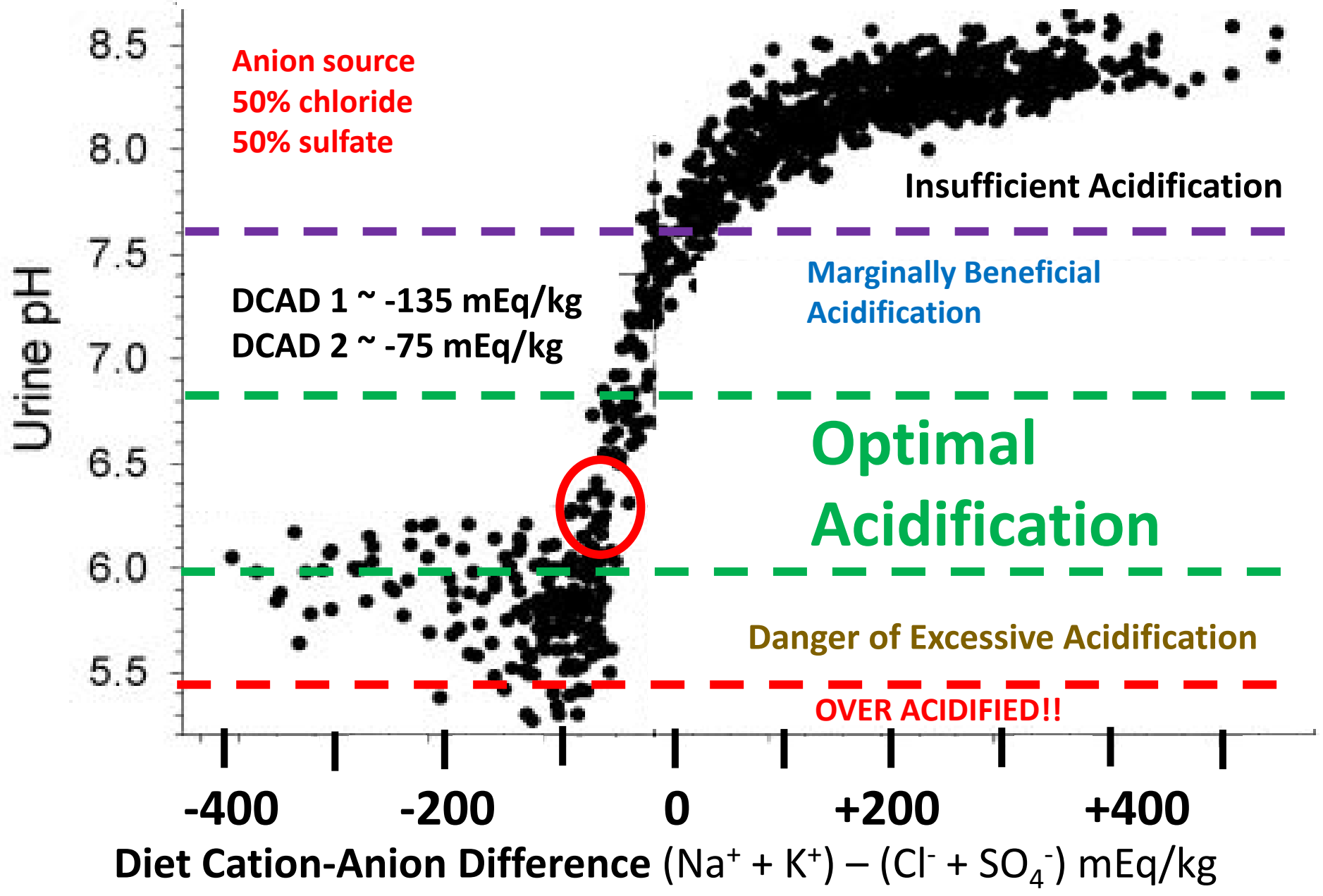

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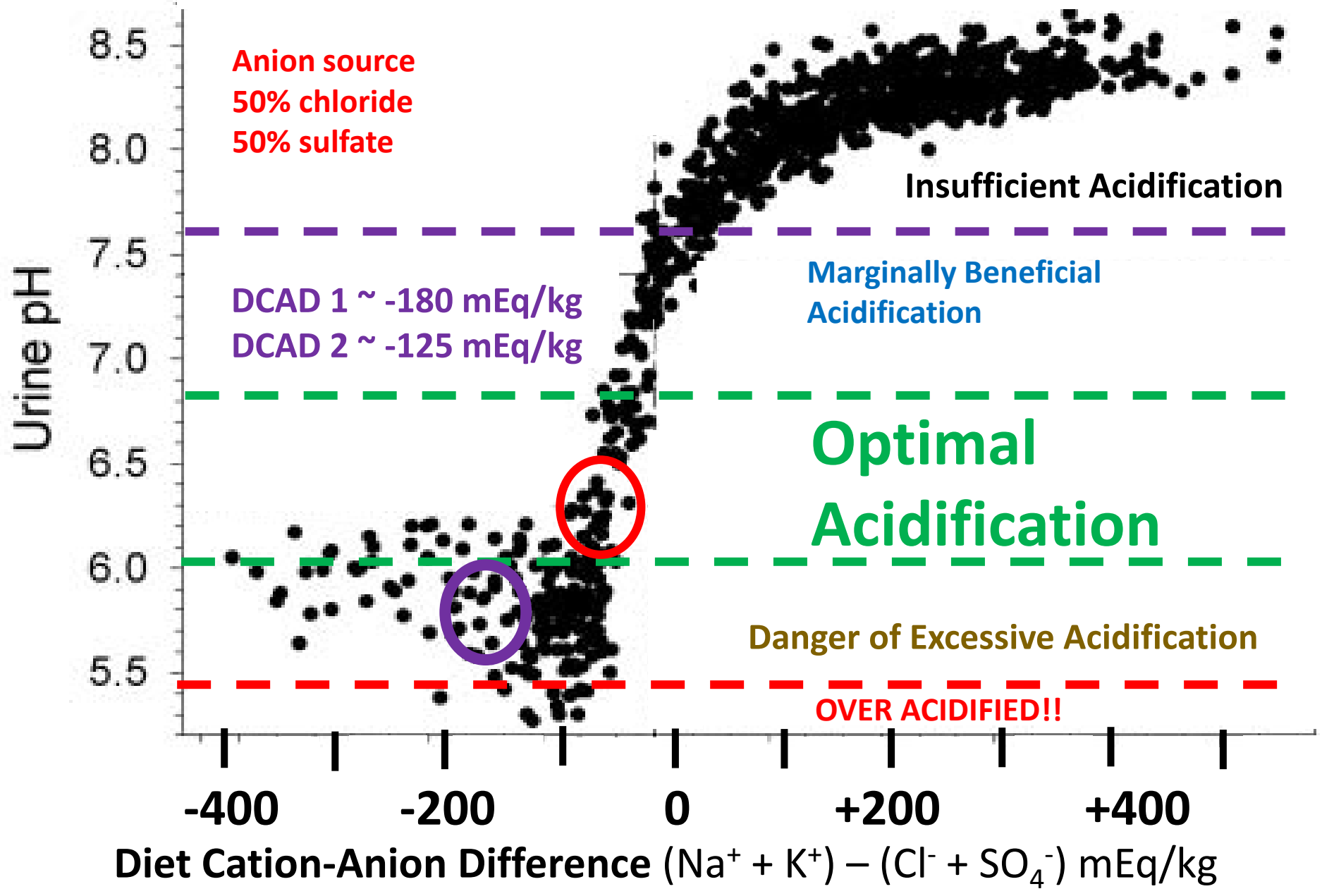

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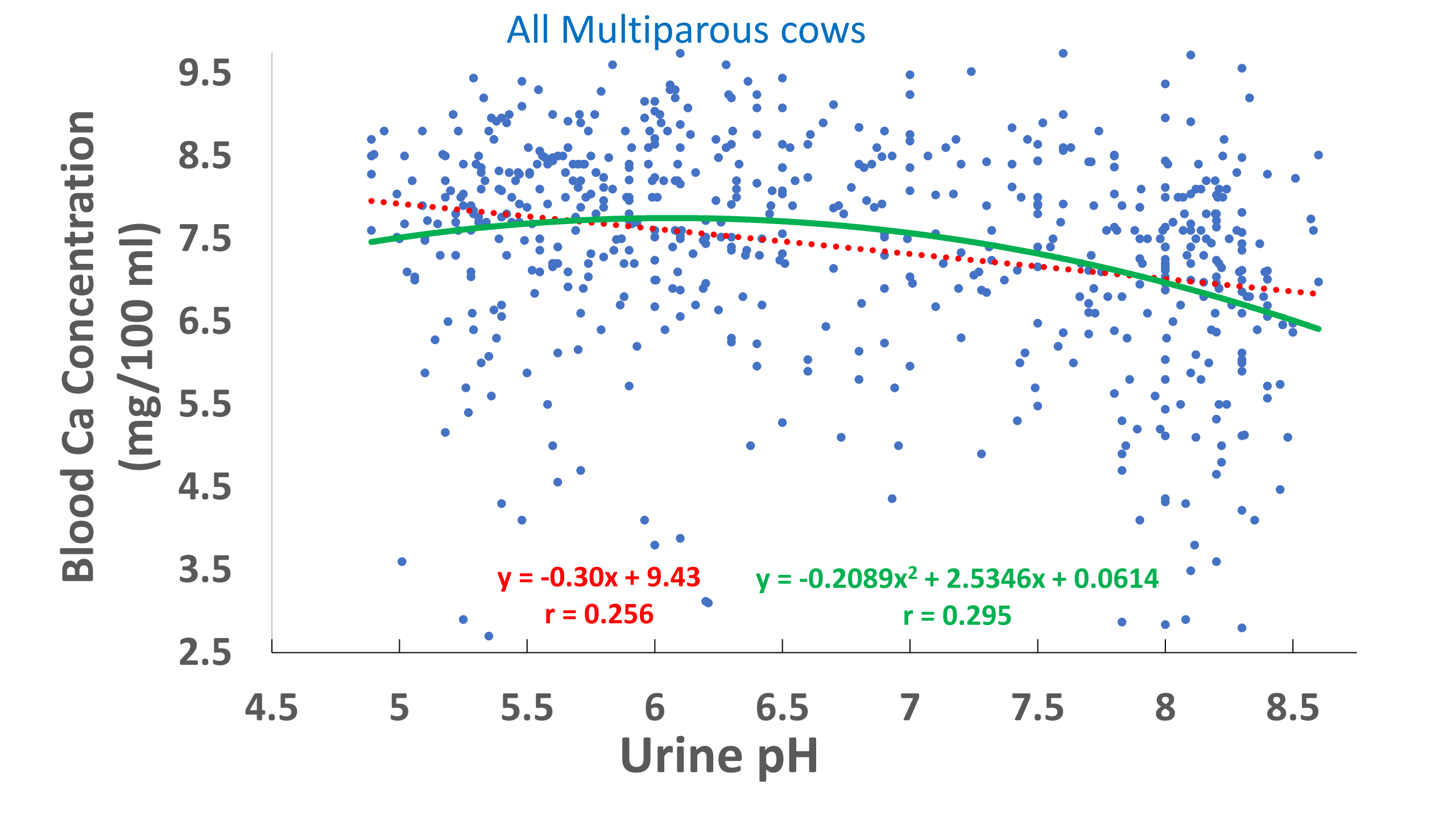
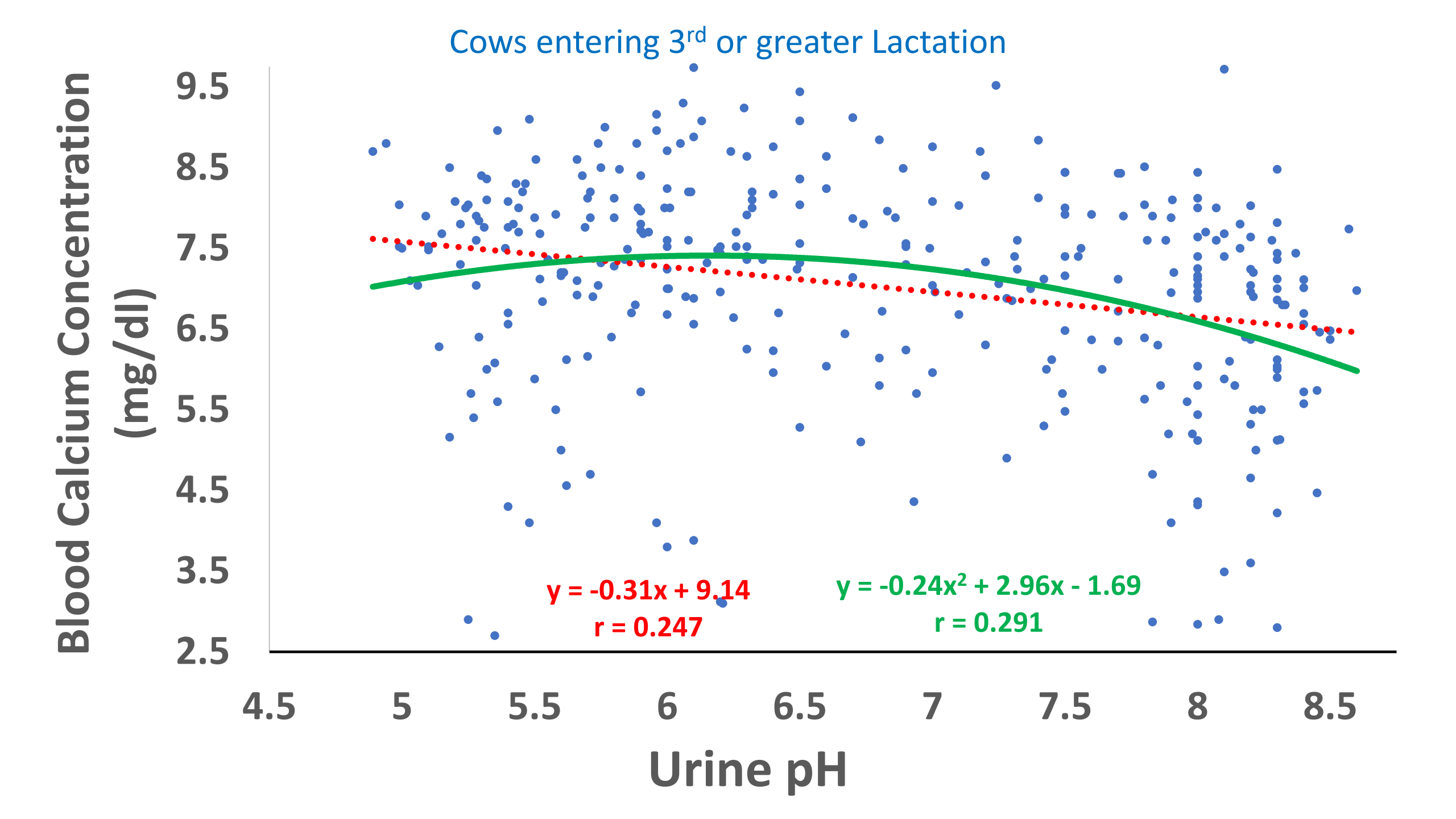
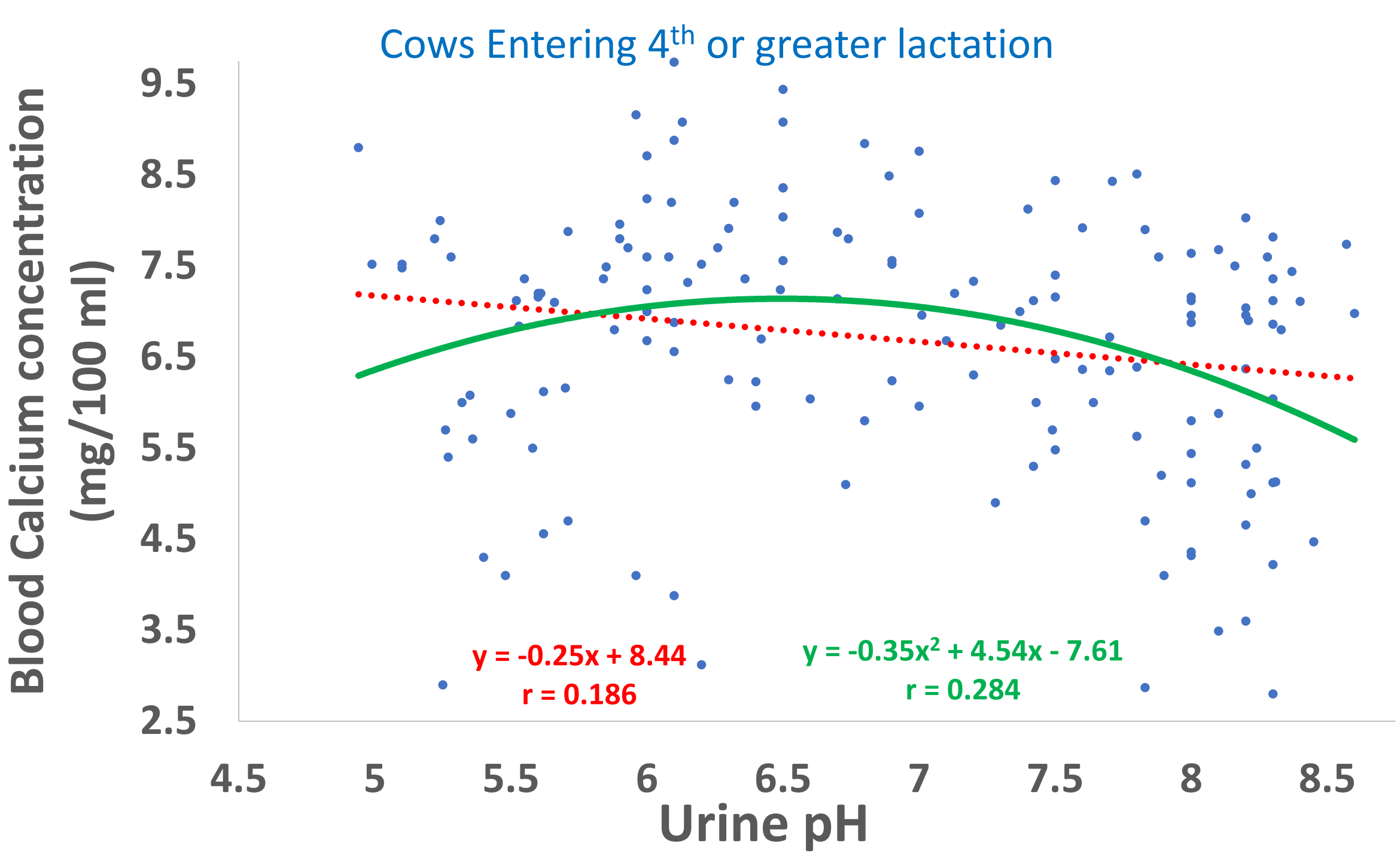
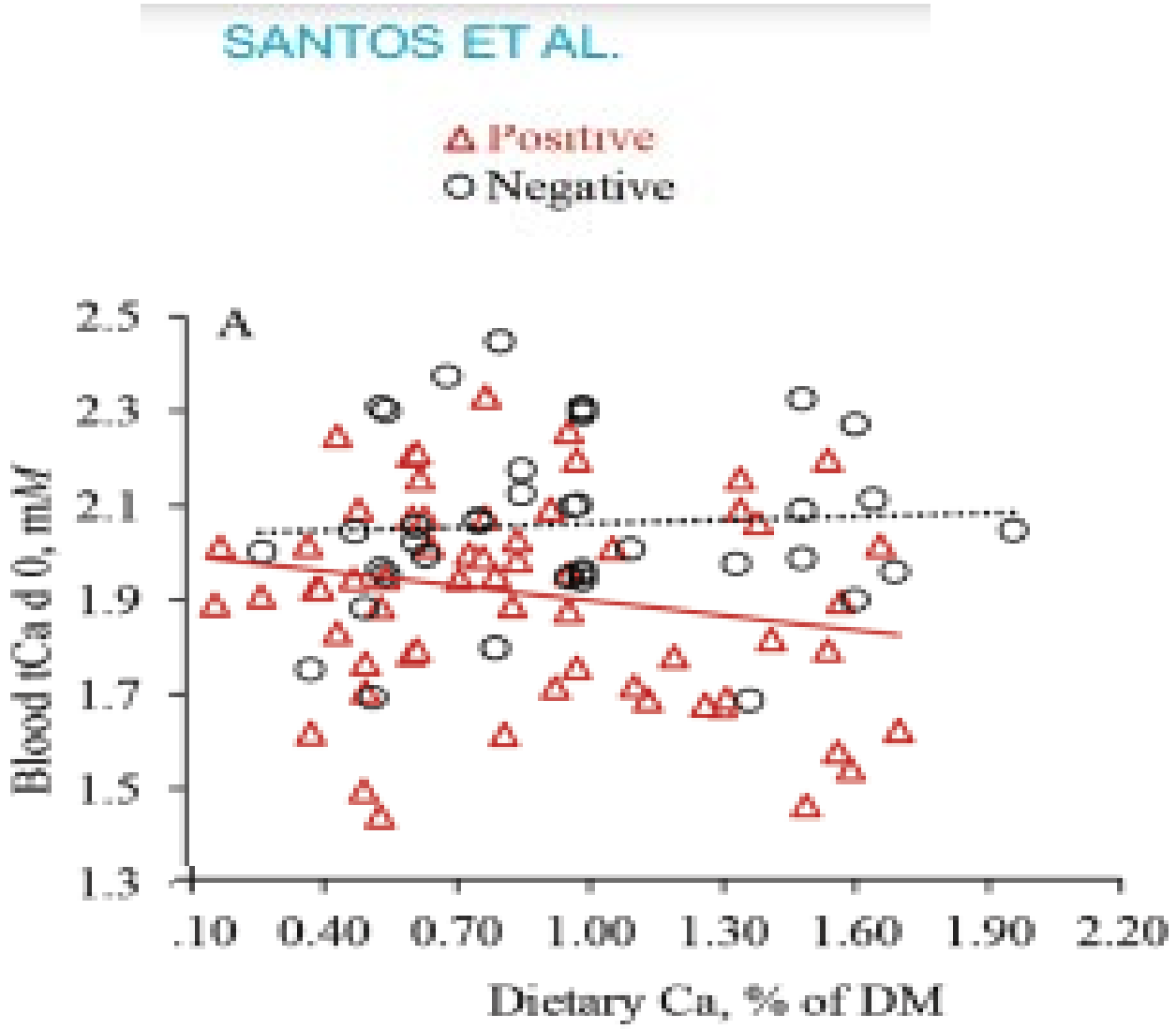

All Multiparous cows
Blood Ca Concentration (mg/100 ml)
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
y = -0.30x + 9.43
r = 0.256
y = -0.2089x² + 2.5346x + 0.0614
r = 0.295
4.5
5
5.5
6
6.5
7
7.5
8
8.5
Urine pH


Cows entering 3rd or greater Lactation
Blood Calcium Concentration (mg/dl)
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
y = -0.31x + 9.14
r = 0.247
y = -0.24x² + 2.96x - 1.69
r = 0.291
4.5
5
5.5
6
6.5
7
7.5
8
8.5
Urine pH


Cows Entering 4th or greater lactation
Blood Calcium concentration (mg/100 ml)
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
y = -0.25x + 8.44
r = 0.186
y = -0.35x² + 4.54x - 7.61
r = 0.284
4.5
5
5.5
6
6.5
7
7.5
8
8.5
Urine pH

How much Ca should I feed with a low DCAD diet???



Santos et al., 2019 Meta Analysis

O = Negative DCAD diet

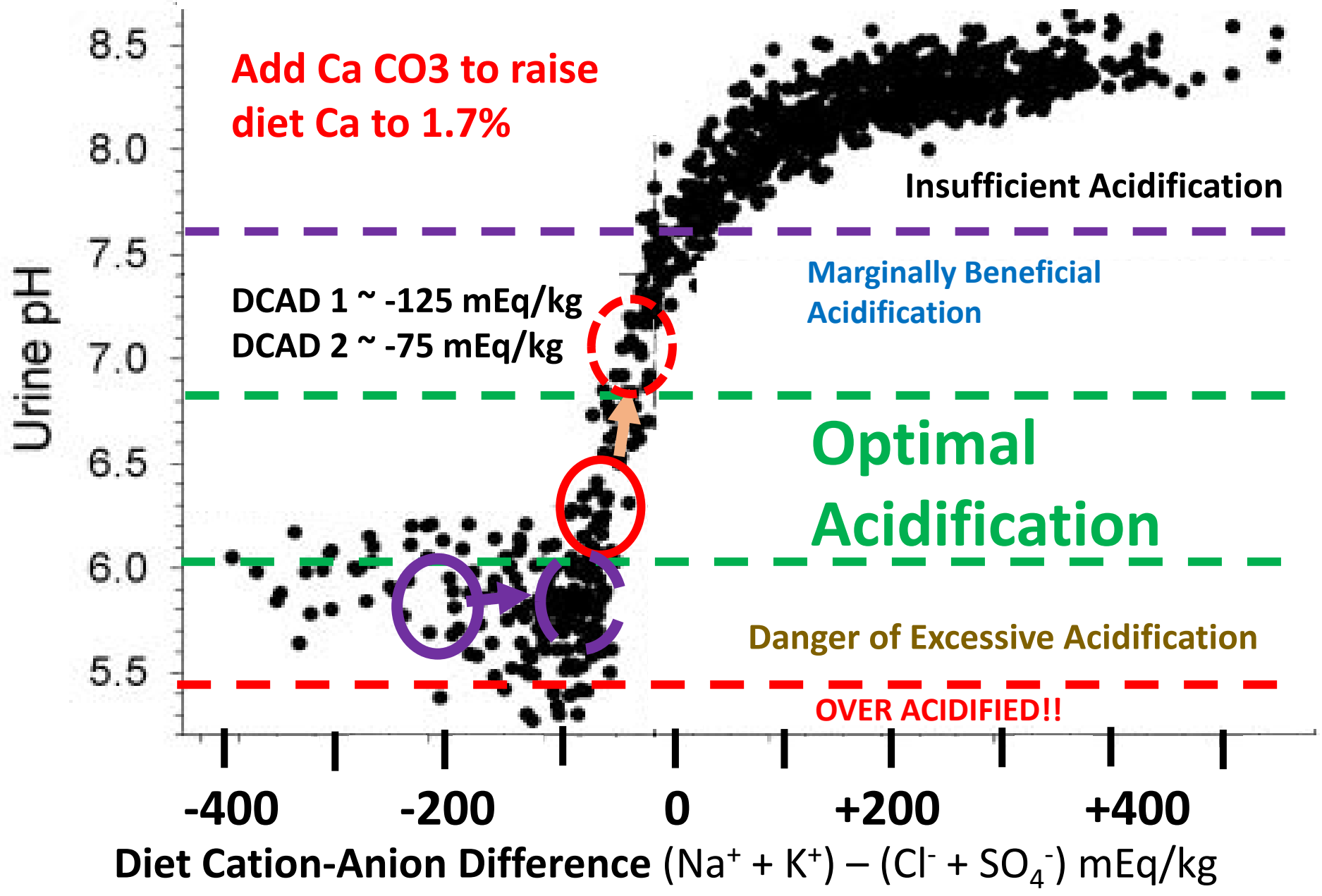
No effect of diet Ca on blood Ca in cows around calving

Δ = positive DCAD diet

Slight decrease in blood Ca when high diet Ca is fed

Limestone has an alkalinizing effect!!!

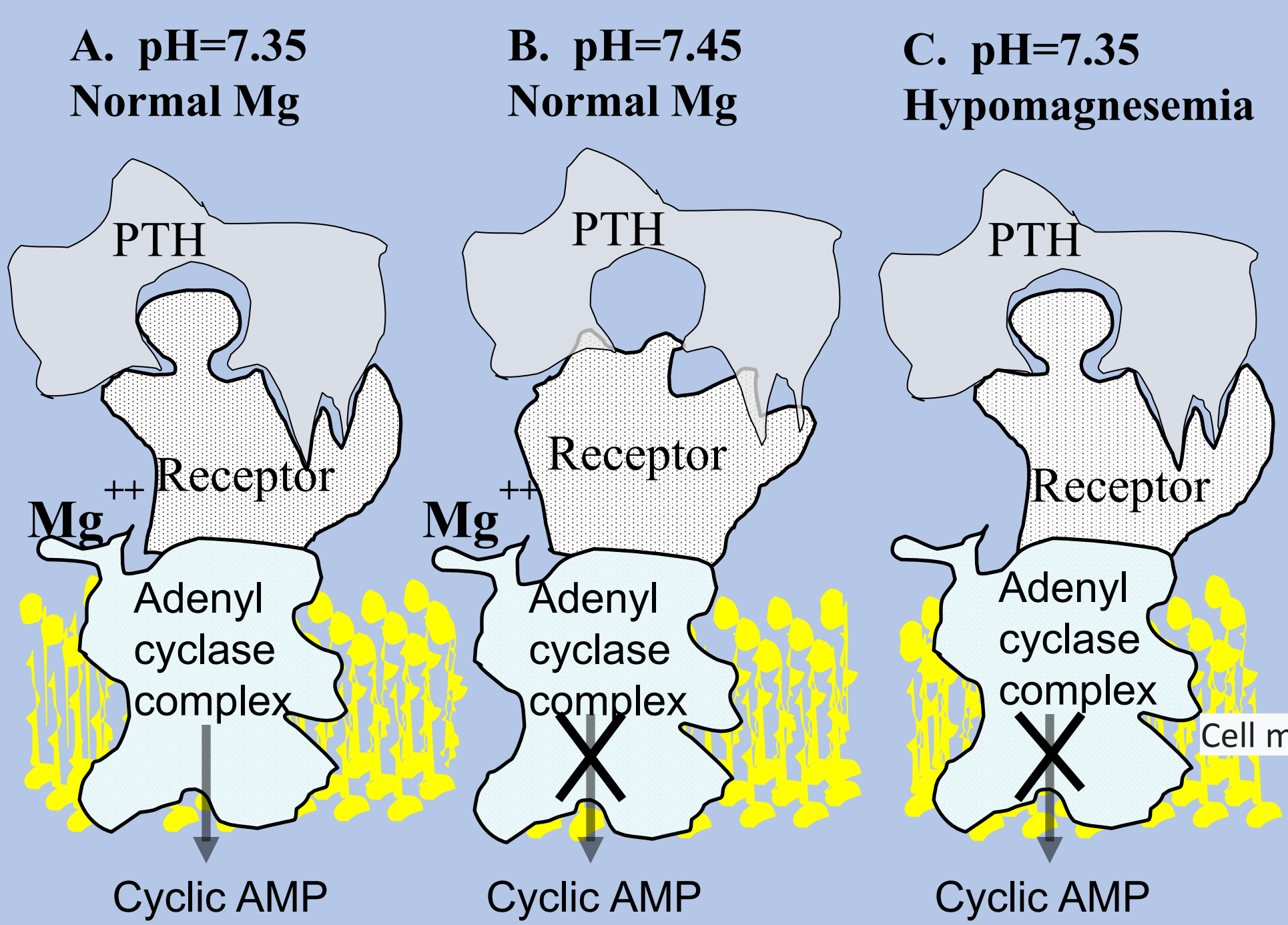
NEED TO FEED MORE ANION TO REACH SAME URINE pH!!



Adapted from Constable et al., 2017; Spanghero, 2004; and Charbonneau et al., 2006

Milk Fever & Hypocalcemia Prevention

1. Avoid very high potassium forages for close-up cows; practiced by most dairies in US.
2. Add anions (Cl or Sulfate) to diet to reduce blood and urine pH; various forms practiced.
3. **Close-up and Fresh cow Diet Mg ~ 0.4%**


A. pH=7.35
Normal Mg
B. pH=7.45
Normal Mg
C. pH=7.35
Hypomagnesemia
PTH
Receptor
++
Mg
Adenyl
cyclase
complex
Cyclic AMP
PTH
Receptor
++
Mg
Adenyl
cyclase
complex
Cyclic AMP
PTH
Receptor
Adenyl
cyclase
complex
Cyclic AMP
Cell membrane

Magnesium – ONLY ABSORBED ACROSS RUMEN WALL

Pre-calving

- using $MgSO_4$ or $MgCl_2$ as “anions” also supplies readily available, soluble Mg.

-The better anion supplements on the market include Mg in this form to remove Mg worries pre-calving.

Post-calving is the bigger issue!!!!!!
Magnesium Oxide – supplies Mg and acts as rumen alkalinizer.

MgO must become soluble to be available for absorption by rumen wall!!!!

Testing Magnesium Oxide Availability

Weigh out 3 g MgO into large vessel.

Add 40 ml of 5% acetic acid (white vinegar) slowly!!

Cap container and shake well and let sit 30 minutes. Check the pH.

Vinegar will be pH 2.6-2.8!

The best MgO will bring the pH up to 8.2.

The worst to just 3.8.

pH is a log scale so this represents >10,000 fold difference in buffering action.

Milk Fever & Hypocalcemia Prevention

1. Avoid very high potassium forages for close-up cows; practiced by most dairies in US.
2. Add anions (Cl or Sulfate) to diet to reduce blood and urine pH; various forms practiced.
3. **Close-up and Fresh cow Diet Mg ~ 0.4%**
4. **Diet P < 0.35%, better below 0.25%**

Excessive Diet Phosphorus Blocks conversion of Vitamin D to the Hormone 1,25-dihydroxyvitamin D

Close-up cow requires diet with 0.22-0.25% phosphorus to be in balance

Above 0.30% Phos begins to impair Ca homeostasis (Wachter et al,2022; Cohrs et al., 2018)

Restricting diet phosphorus below requirements can reduce hypocalcemia (Kichura et al., 1982).

Addition of Na aluminosilicates (zeolites) to diets can bind enough phosphorus to reduce hypocalcemia (Thilsing-Hansen et al., 2002)

Keeping Phosphorus Low

Do not add any source of mineral phosphate such as dicalcium phosphate. Check mineral pack!!

Take care when using canola meal as protein source for close-up cows

- canola meal phos = 1.05 % DM basis
- Soybean meal phos = 0.55% DM basis

Zeolite A (Thilsing-Hansen, et al. 2001)

In a test tube the sodium aluminosilicate can bind 1 g of Ca for every 10 g zeolite.

Creates a Low Ca diet to stimulate PTH release well before calving

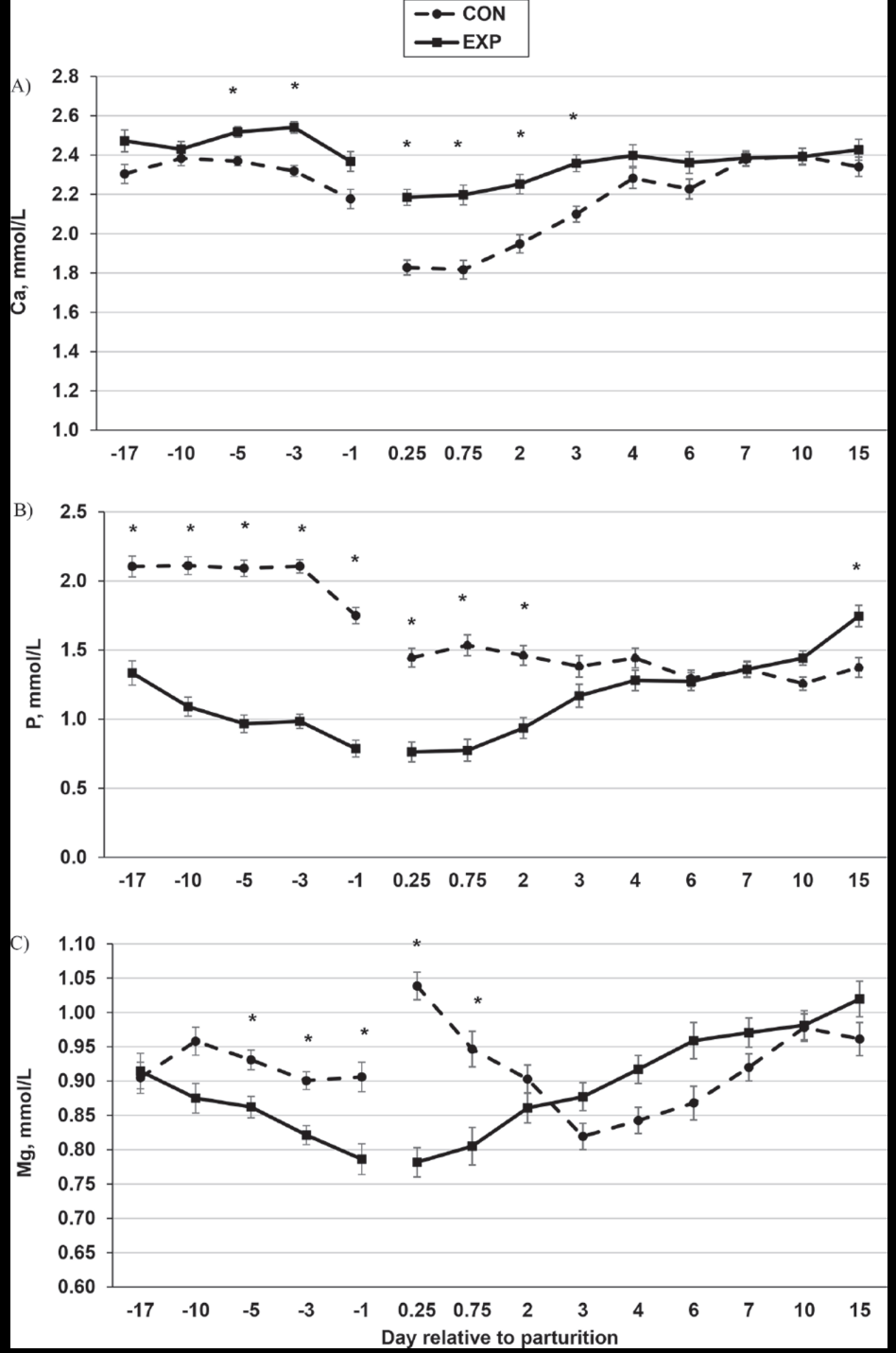
Binds phosphate and magnesium as well. Trace minerals?? Transient reduction in blood Mg and Phos.

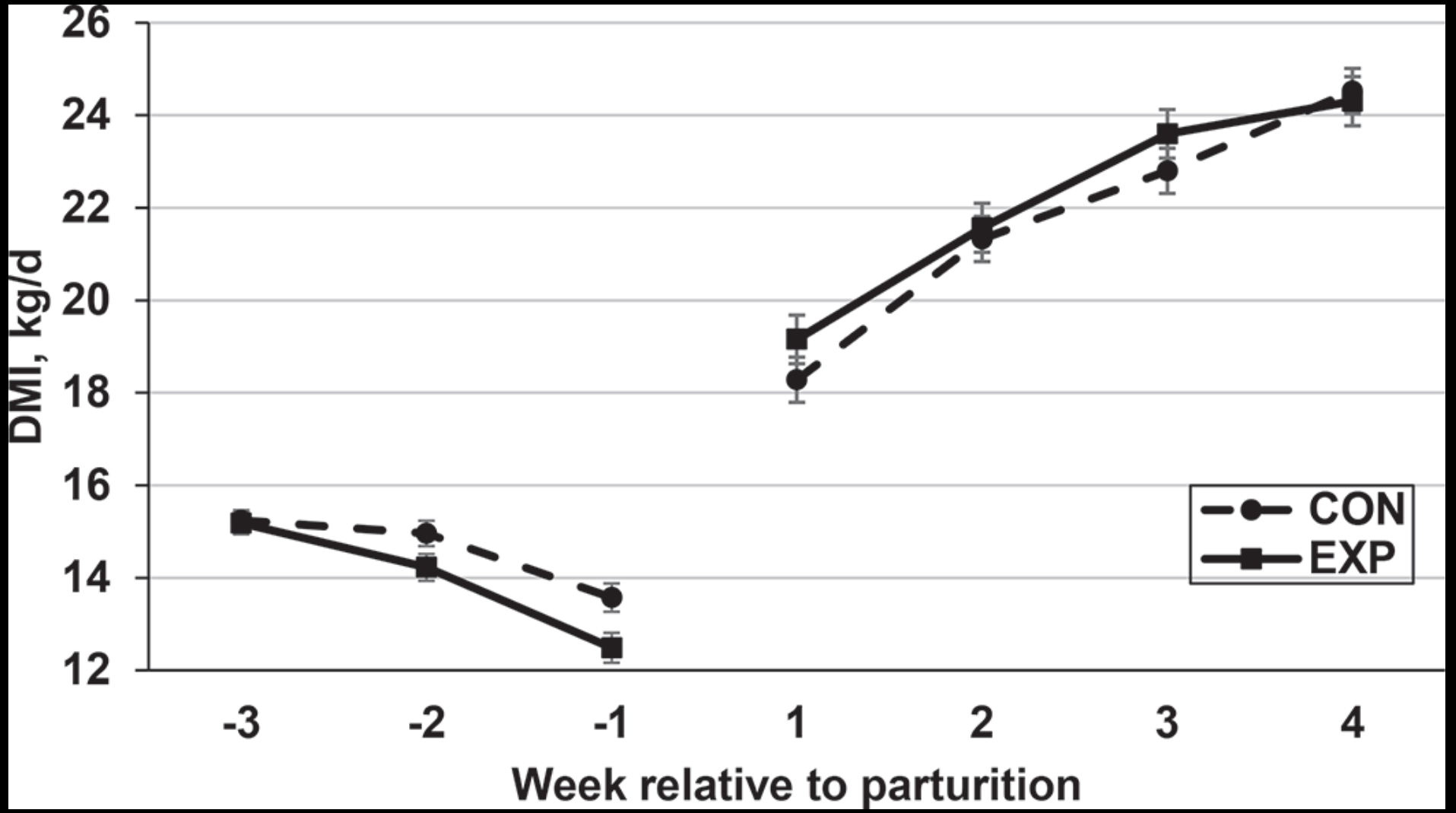
Lower blood phosphate may be an important aspect to its mechanism of action!!!

Kerwin et al., 2019

Added 0.5 kg zeolite to a diet that was :

0.65 % Ca ,
0.39% Phos,
0.42% Mg
DCAD of + 268 mEq/kg





DMI Treatment X week P= 0.04

Rumination rate significantly decreased with zeolite prepartum. P=0.03

Zeolite

ADVANTAGE

No need to restrict diet Potassium

Urine pH testing not necessary

DISADVANTAGES

Cost

Often reduces Dry Matter intake.

Unlikely to work well should diet Ca rise above 0.7%.

- must take care to restrict Ca found in TM/ Vitamin Packs.

Does binding of Mg and trace minerals have any impact on health?

Impact of Reducing DCAD on health and milk production

Lean et al., 2019. Santos et al., 2019. Meta-analysis indicates significant beneficial effects (P<0.02) on:

Milk Fever, Blood Ca (the day of calving and "postpartum"), Retained Placenta, Metritis, and risk of Multiple Health Events

But not Mastitis (P=0.63) and LDA (P= 0.73)

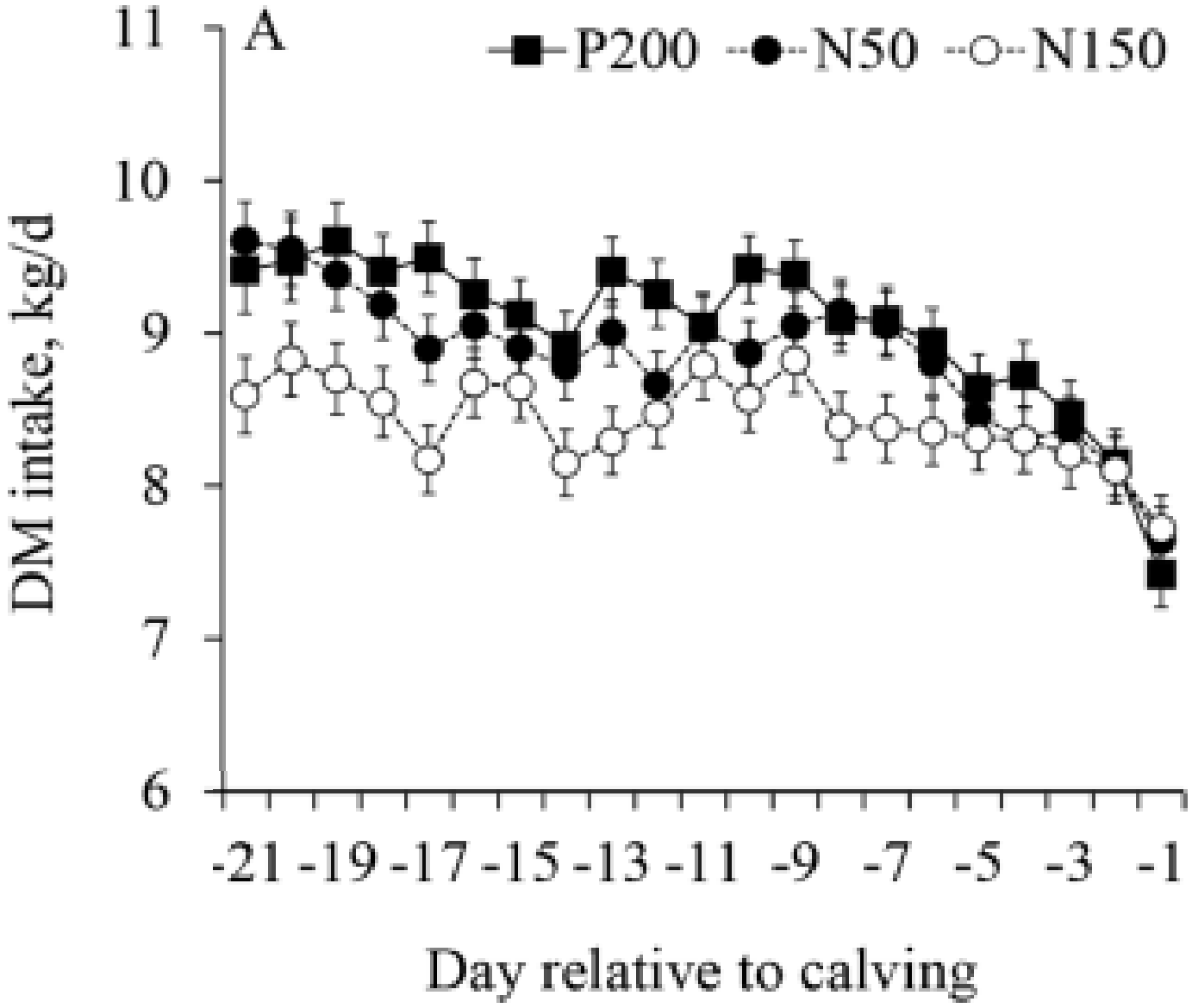
Milk Production – Multiparous → + 1.1 to 1.7 kg/day

Nulliparous → - 1.28 to - 1.4 kg/day!

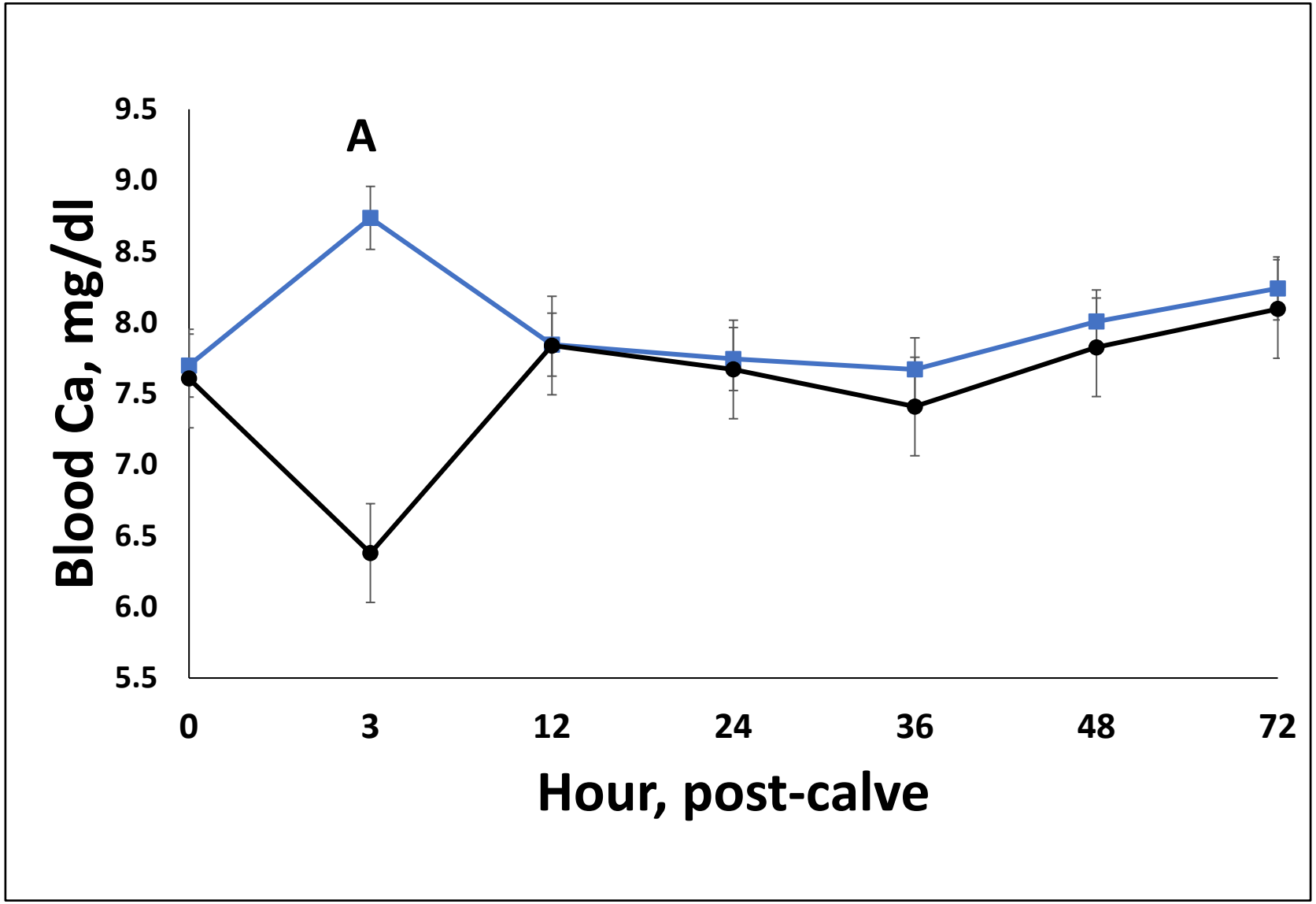
Zimpel et al. 2021 (a,b) - compared to No Anion Controls, negative effects on heifers not observed if "moderately low DCAD" was fed with urine pH 6.67 vs 5.41

Zimpel et al., JDS 2021

Effect of DCAD on dry matter intake before calving in Nulliparous cows.
(Na + K) - (Cl + S)



Oral Ca boluses can support blood Ca for about 3-6 hrs and likely need to be repeated



Oral Calcium boluses PLUS anionic diets????

DCAD Adjustment with added anions

To take a diet from +200 mEq/kg to -100 mEq/kg would require the addition of 300 mEq chloride / kg diet DM. And if cows eat 13.5 kg DM/day that amounts to adding 4050 mEq chloride to the diet each day

Bolus containing 40 g Ca as calcium chloride supplies 2000 mEq of chloride.

One calcium bolus adds about ½ a days worth of anion!!!

OVERACIDIFICATION POSSIBLE!!!

Fresh Cow Diets – The Next Frontier

What's the matter with the high group TMR??

What changes should be made from the HIGH group TMR diet?

How long should they be fed??

My Opinion -changes to be made from the HIGH group TMR diet?

Energy – starch same as high group, more straw → LDA prevention?

Protein – 19-20% CP And amino acid balanced!!

Fat - Don’t add any!

Calcium – higher, 1.0-1.2% Ca

Magnesium – higher, 0.45-0.5% and available MgO, MgOH2, MgCO3

Vitamin E – higher, 3000-4000 IU /day