Transition cow management: calcium health and diagnostics

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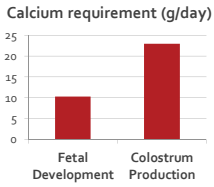
Overview

- Background of hypocalcemia
- Classification of subclinical hypocalcemia – is it abnormal?
- Measurement methods
- Current testing recommendations

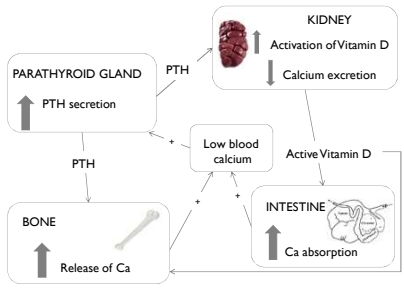
Large demand for calcium

- Sudden increase in requirements
  - Need ~24 g for colostrum
  - Only 2-4 g in plasma pool
- Adaptation requires coordination of several hormones and tissues
- Daily calcium requirement for 100 lbs milk = 50 g



Courtesy: Brittany Leno

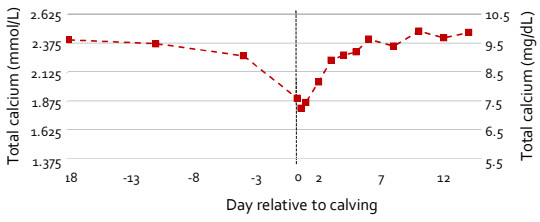
Increasing blood calcium



Goff et al., 2008

Courtesy: Brittany Leno

Periparturient change in blood calcium

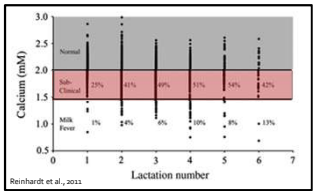


Sweeney et al., 2015. J. Dairy Sci 98 (Suppl. 2):128

Courtesy: Brittany Leno

Today's hypocalcemia

- Clinical disease has been well addressed, focus now on subclinical disease



- Milk fever incidence <5% on dairies
- Subclinical hypocalcemia (SCH) incidence up to 50%

Classification of SCH at calving

J. Dairy Sci. 101:547–555
https://doi.org/10.3168/jds.2017-13313
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Association of immediate postpartum plasma calcium concentration with early-lactation clinical diseases, culling, reproduction, and milk production in Holstein cows

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- *Objective*: to determine the association of plasma total calcium (tCa) collected soon after parturition with:
  - Health outcomes (RP, metritis, DA, clinical mastitis)
  - Culling risk within 60 DIM
  - Pregnancy risk to 1st service
  - Milk production across the first 9 DHIA tests

Neves et al.: materials and methods

- Prospective cohort study in 5 dairy herds in NY
  - Part of a large randomized clinical trial
  - Control cows only

- Enrolled cows that calved between February-November, 2015

	Farm				
	A	B	C	D	E
Milking cows, n	1,474	567	1,282	1,677	1,222
Milk production, kg	38.4	38.9	37.0	37.3	36.8
Prepartum DCAD, mEq/100 g DM	-6.9	-2.8	-5.5	7.3/14.1	-2.8

Neves et al.: results

- n = 1,416 included in the final analysis
  - Primiparous, n = 350
  - Multiparous, n = 1,066
- Mean time from calving to blood collection = 3 h

	Primiparous	Multiparous
Retained placenta	6.0%	9.2%
Metritis	13.0%	8.9%
Displaced abomasum	0.3%	3.7%
Clinical mastitis	4.6%	10.0%
Culling	2.6%	4.9%
Pregnancy to 1st service	44.5%	37.3%

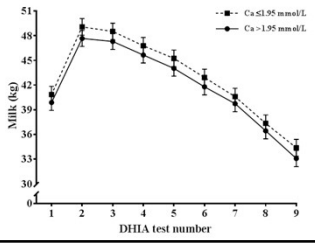
Neves et al.: results

- Primiparous cows: tCa at calving meant nothing!

- Multiparous cows:
  - tCa **not** associated with: risk of RP, metritis, clinical mastitis, or pregnancy to 1st service
  - tCa ≤1.85 mmol/L:
    - More likely to develop a DA
    - RR = 2.8 (95% CI = 1.35 to 5.85; *P* = 0.006)
  - Higher Ca associated with increased culling risk
    - Every 0.1 mmol/L increase, RR = 3.4 (95% CI = 0.95 to 12.0; *P* = 0.06)

Neves et al.: results

- Multiparous cows with tCa ≤1.95 mmol/L:
  - Made more milk: 42.9 vs. 41.8 kg per test-day, *P* < 0.001



Neves et al.: conclusions

- Caution in classifying SCH based on a single time-point collected within 12 h of calving
- Are our cut-points for SCH too high?
- Is it the duration of SCH, not the value that is important?

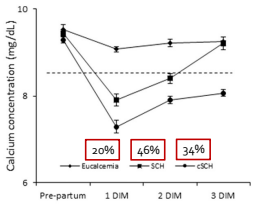
Chronic subclinical hypocalcemia (cSCH)

Theriogenology. 2017 May;94:1-7. doi: 10.1016/j.theriogenology.2017.01.039. Epub 2017 Jan 25.

Association between subclinical hypocalcemia in the first 3 days of lactation and reproductive performance of dairy cows.

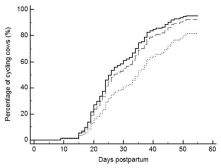
Caixeta LS[1], Ospina PA[1], Capel MB[2], Nydam DV[3].

- 2 dairy farms, 97 cows
- Definitions:
  - SCH = serum tCa ≤2.15 mmol/L (8.6 mg/dL)
  - cSCH = SCH at 1, 2, and 3 DIM
- Incidence cSCH:
  - Parity 1 = 20%
  - Parity 2 = 32%
  - Parity ≥3 = 46%



Caixeta et al.: chronic SCH on reproduction

- Return to cyclicity:
  - Eucalcemic cows were more likely to return to cyclicity by end of VWP than cSCH cows
  - HR = 1.8 (*P* = 0.06)



- Pregnancy at first service:
  - cSCH cows had lower odds of pregnancy compared to eucalcemic cows
  - OR = 0.27 (*P* = 0.04)

Is subclinical hypocalcemia bad?

- When to test?
  - Not at calving
  - Need more longitudinal studies with lots of cows
- What cut-point to use?
  - Large, epidemiological studies to define "normal"
  - Based on health and production outcomes
- How do we test cows?

Determining Calcium Status

Cold ears?

J. Dairy Sci. 99:6542–6549
http://dx.doi.org/10.3168/jds.2015-10734

Evaluation of ear skin temperature as a cow-side test to predict postpartum calcium status in dairy cows

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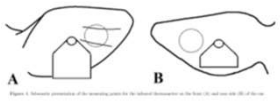
†Veterinary practice G. Thiele, Baruth, Germany

- 7 herds
- 251 cows, 0-48 hr postpartum
- Manual scoring
- Rectal temperature
- Infrared thermometer
- Blood calcium



- Hypocalcemia defined as blood calcium < 2.0 mmol/L

Calcium threshold, mmol/L	Prevalence, %	Temperature variable[1]	Threshold, °C	Sensitivity	Specificity	AUC[2]	*P*-value
2.0	29.6	STEar	27.0	49.3	73.8	0.641	0.001
		STCox	30.0	52.2	78.7	0.668	0.001
		RT	29.0	75.4	42.7	0.606	0.009

- Decrease in ear temp of 0.39°C associated with decrease of 0.1 mmol/L in calcium
- Ambient temp was a major confounder
- Conclusions: ear temperature cannot be recommended for diagnosis of subclinical hypocalcemia

Direct measurement of calcium

- Calcium is differentiated into 3 forms in blood:
  - Free or ionized (50-60%)
  - Bound to proteins (30%)
  - Complexed (10%)
- 2 options:
  - Total calcium (tCa)
  - Ionized calcium (iCa)

Total calcium

- Collect in green or red top tubes
- Fairly stable
- Methods of analysis:
  - Benchtop analyzer in laboratory @ $5-15/sample
  - Analyzer in vet clinic @ $5-7.50/sample

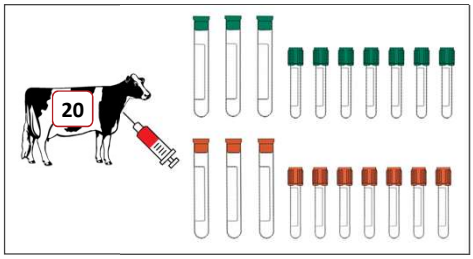
Stability of total calcium measurement: best practices for bovine practitioners

AABP-L: *I'm working with a dairy client on some transition cow issues and we'd like to do some hypocalcemia screening of fresh cows. This dairy has herd check every two weeks and is an hour away. They are taking blood after first milking and storing red top tubes in fridge until next herd check. Thus when I collect them, the samples will be 1-14 days old. The dairy does not have a centrifuge. How should the red tops be stored--fridge or freezer or other?*

Responses (paraphrased):

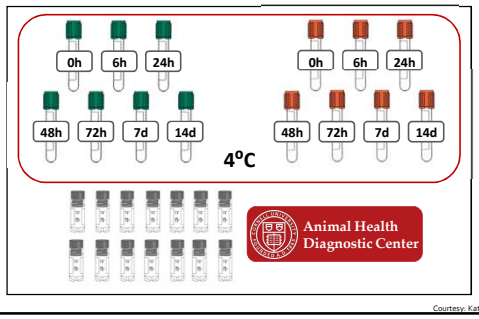
- Use serum separator tubes, let them clot in a refrigerator for few hours, the wax plug will separate the serum from red cells. These tubes should be stable for some time in the fridge.
- The best solution is to collect in a red top tube and turn the red top tube upside down in the fridge for at least 8 hours. Set them upside down at a slight angle in the fridge so the clot forms in the depression of the red rubber top. Once the clot is completely formed, hold the tube so the rubber top can be removed gently, and pull the entire clot out while keeping the serum in the tube. Serum may be frozen or kept in a fridge if it will be picked up in a few days.
- In my opinion, there isn't a huge effect by age of sample on Ca assay. Store the samples in the fridge upside down, and after a couple of days, gently turn the vials upright and pull the stopper. The clot should stick to the stopper and can be discarded. Re-stopper the sample.

Study design



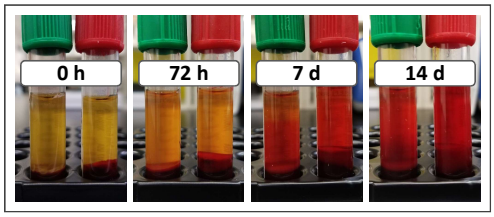
Courtesy: Kathryn Bach

Study design



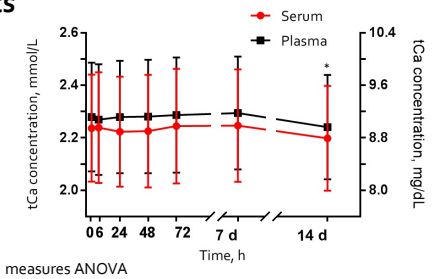
Courtesy: Kathryn Bach

Results



Courtesy: Kathryn Bach

Results



- n = 13
- Repeated measures ANOVA
  - Time, $P < 0.001$
  - * = different from Time 0, $P < 0.05$
  - Sample type, $P = 0.64$

Ionized calcium

- iCa thought to have greater biological relevance than tCa
- Ion-selective electrode technology is largely employed for clinical use (blood-gas analyzers)
- Measurement of iCa is expensive, special handling procedures
  - Heparin salts bind calcium
  - Use of electrolyte-balanced syringes
  - Exposure to air changes blood pH

Ionized calcium – methods of analysis

- Cowside = not practical
- Machines targeted for on-farm use:
  - iSTAT, VetScan, Nova Stat
  - $5,000-$15,000 + sample costs
- Fast, accurate, and inexpensive tools that measure iCa are currently non-existant
- Why not just measure tCa?
  - Relationship between tCa and iCa varies following parturition (Leno et al., 2017)

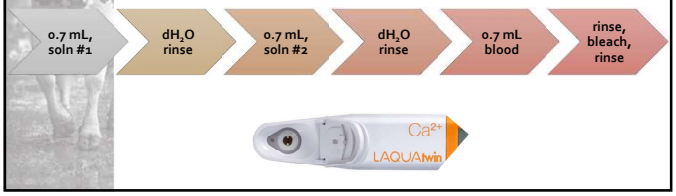
Optimization of commercial meter

Dr. Rafael Neves

- Software changes: units and resolution
- Modification of calibration set-points
- Temperature sensor adjustments

Final prototype

- 2 calibration solutions: 1.25 mmol/L, 5.0 mmol/L
- 15 sec sample contact time
- 0.7 mL blood



On-farm vs. in-lab comparison

Blood collected into a plain vacutainer tube

Results obtained on-farm (fresh whole blood)

Results obtained in the lab (hep-balanced syringe)

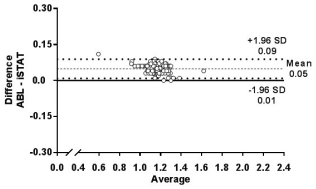
vs.

101 cows from 3 herds

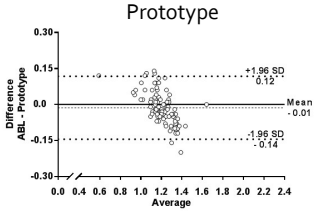
Courtesy: Rafael Neves

On-farm vs. in-lab comparison

i-STAT



Prototype



Bland-Altman plots

Courtesy: Rafael Neves

On-farm vs. in-lab comparison

Method	SCH cut-point (mmol/L)					
	≤0.95		≤1.00		≤1.05	
	Se (%)	Sp (%)	Se (%)	Sp (%)	Se (%)	Sp (%)
Prototype	100	98	100	96	100	97
i-STAT	100	97	100	97	100	93.5

- SCH based on the heparinized-balanced syringe sample analyzed in the ABL-800 FLEX
- Wide Se confidence intervals - few low iCa samples

Precision

- Coefficient of variation: 10 consecutive measurements
- Below, within, and above normal iCa range

iCa concentration	Coefficient of variation
0.72 mmol/L	3.9%
1.29 mmol/L	2.1%
2.0 mmol/L	1.0%

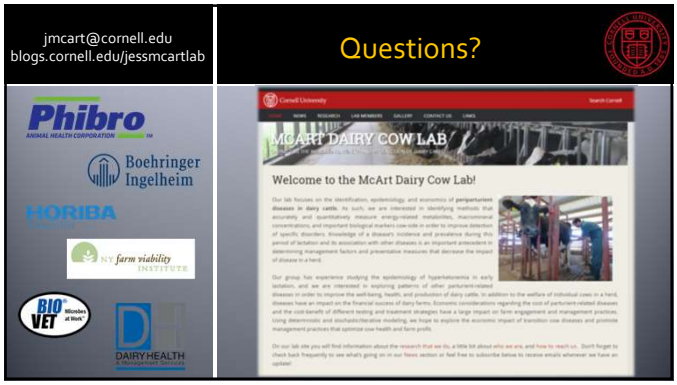
On-farm Horiba iCa meter?

- Not a good quantitative meter: mmol/L
- Solid qualitative meter: yes/no
- Future:
  - Release date by Horiba unknown
  - Develop quality-control check
  - Need to streamline on-farm use

Dr. Rafael Neves & Dr. Kathryn Bach

Current testing recommendations

- Wouldn't it be great if I could tell you this …
- We need better on-farm measurement tools
  - Who
  - When
  - What
- Improve monitoring of our preventative methods
- Improve and target treatment methods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