Circadian Rhythms and Feed Management

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2019 Herd Health and Nutrition Conference

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Circadian/Daily Rhythms in the Dairy Cow

- Circadian rhythms are 24 hour repeating cycles

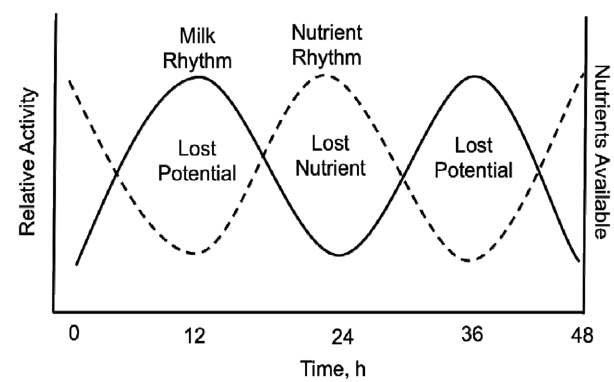
- Many biological functions follow a 24 cycle
  - Activity and Alertness
  - Nutrient Metabolism
  - **Milk Synthesis**
  - **Intake**

Why??
Allows the animal to anticipate changes and adapt before they occur

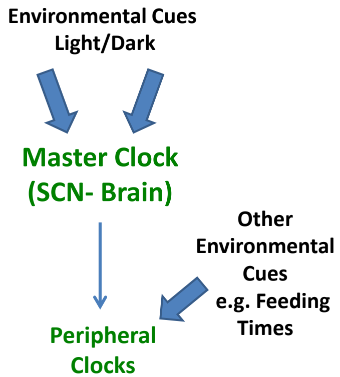
Key Principles

- There is a daily (circadian) pattern of intake that has a major impact on the rumen
- There is a daily pattern of milk synthesis
- Maximizing efficiency requires synchronizing nutrient absorption and mammary needs
- Considering daily patterns provides opportunities to optimize milk production

Are the Daily Patterns of Nutrient Absorption and Milk Synthesis Synchronized?



How Does the Cow Know What Time of Day It Is?



- **Main environmental cues:**
  - Light/Dark
  - Feeding Times
  - Milking Time?
- **A disconnect between environmental cues can cause metabolic issues in humans and rodents**

- This occurs in restricting feed to the day in nocturnal animals and night shift work in humans

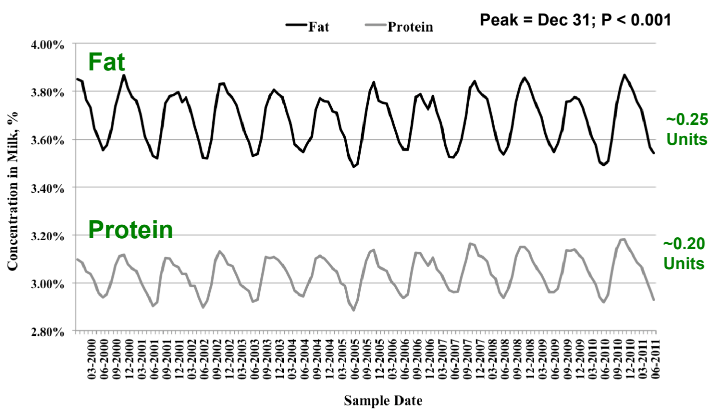
Asher, Schibler 2011

Seasonal Rhythms are Also Common in Biology

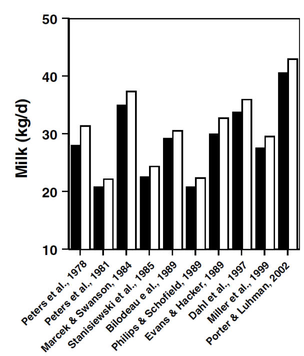
- **Patterns that repeat every year**
- **Mostly driven by day length and/or changes in day length**
- **Regulated through the same molecular system as circadian rhythms**

Some Amazing Examples in Biology

Seasonal Pattern of Milk Fat & Protein:
Mid East US Milk Market



Long day photoperiod increases milk yield and milk fat yield, generally with no change in milk fat percent



Dahl and Petitclerc., 2003

-16 to 18 hr vs. 8 to 10 h light

~5 to 10% increase across all production levels

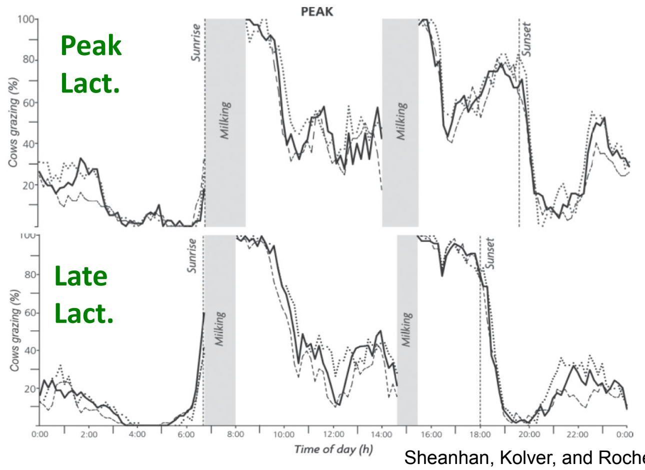
Continuous Light is the Same as Natural Daylight!!!!

- Milk yield is maximized by short days during the dry period

- Also likely through molecular mechanism of circadian regulators

Is There a Circadian Pattern of Intake?

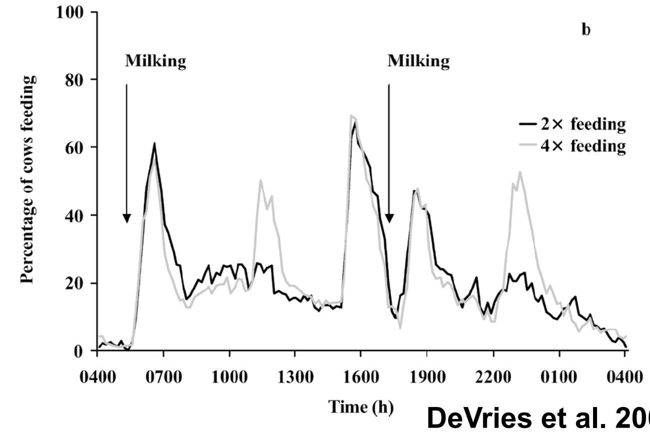
Pasture Fed Cows



Sheanhan, Kolver, and Roche, 2011

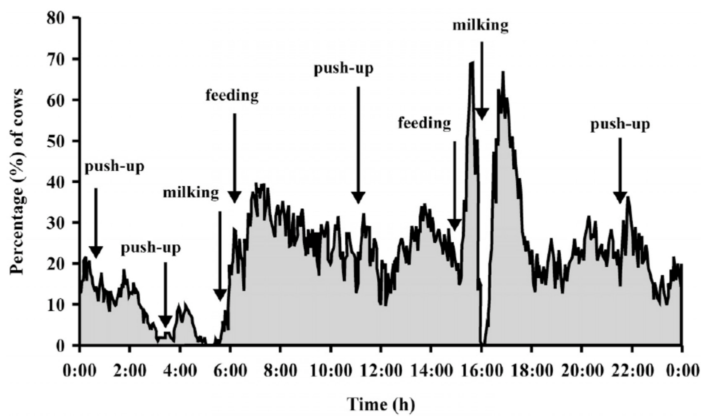
TMR Fed Cows: Feeding and Milking Times are Important

Feeding and milking commonly both near dawn & dusk in experimental data



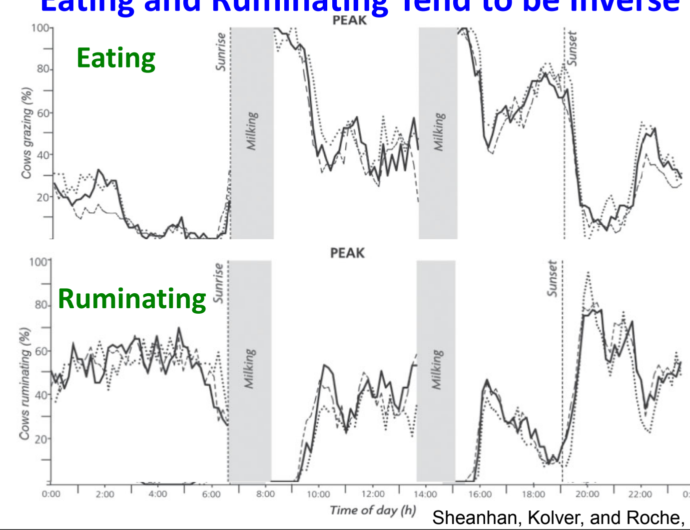
DeVries et al. 2005

Pushing Up Feed Has Less Influence



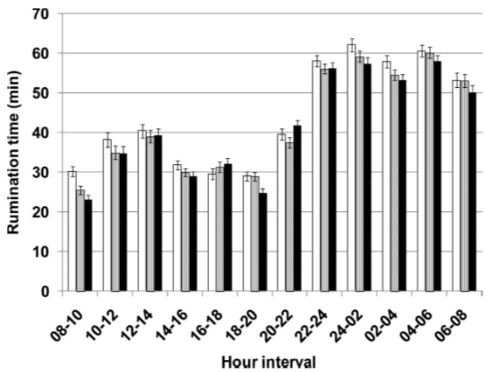
DeVries et al. 2003

Eating and Ruminating Tend to be Inverse



Sheanhan, Kolver, and Roche, 2011

Rumination Pattern

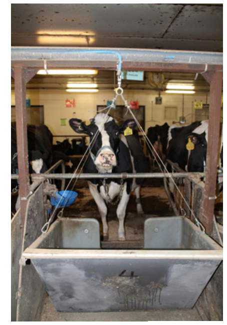


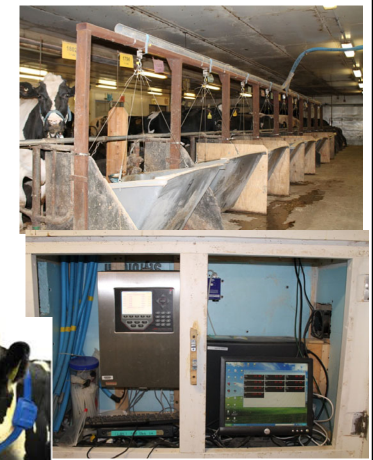
Low, Medium, and high Temperature-Humidity Index

Daily pattern of rumination time expressed in minutes per 2 h in 3 levels of daily maximum temperature-humidity index (THI).
White bars = THI <80; bars with vertical lines = THI from 80 to 85; black bars = THI >85.

Soriani et al. JDS 2014

PSU Feeding Behavior System

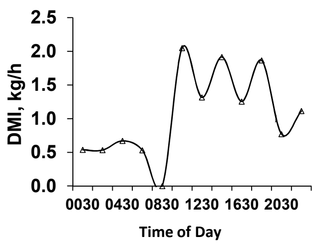


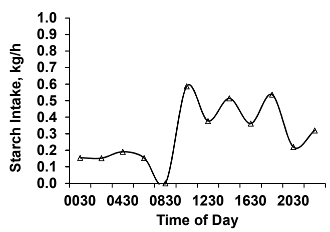


MooMonitor+ Dairymaster

(Image Dairymaster.ie)

Rate of Feed Intake is Variable Over the Day





Ying et al. 2015

What is the Impact of the Daily Pattern of Intake

Intake =

Entrance of fermentable organic matter into the rumen

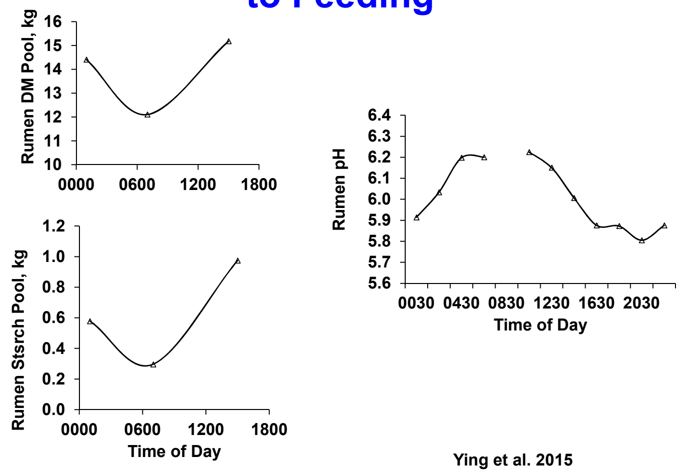
Fermentable organic matter =

Synthesis of VFA's & microbial protein

VFA's =

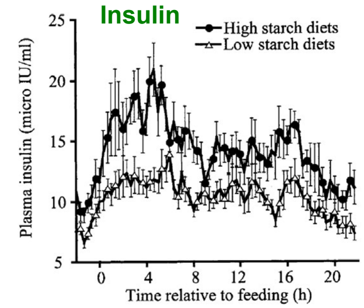
Rumen Acid Load
&
Nutrient supply for cow

Rumen Pool Size Changes Relative to Feeding

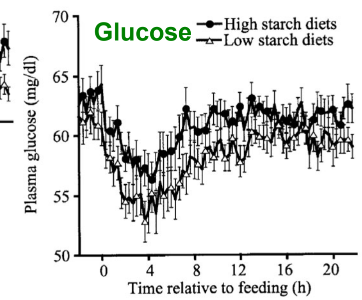


Ying et al. 2015

Intake Creates a Circadian Pattern of Plasma Metabolites and Hormones



Oba and Allen, 2003



How Flexible is the Daily Pattern of Feed Intake?

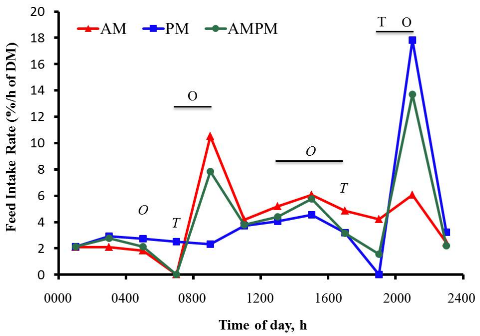
- **Feeding stimulates intake, but what is the impact of feeding time**
- **Fed TMR:**
  - **1x/d at 0830 h (AM)**
  - **1x/d at 2030h (PM)**
  - **2x/d at 0830 and 2030 h (AMPM)**

DMI and Milk Production

	Treatment LS-Means				*P*-value	-----Contrasts-----	
Item	AM	PM	AMPM	SE	Trt	AM vs. PM	AM vs. AMPM
Yield, lbs/d							
Milk	110.0	111.1	111.8	5.7	**0.69**	**0.59**	**0.40**
Milk fat	3.78	3.78	3.85	0.09	**0.84**	**0.99**	**0.62**
Milk protein	3.26	3.28	3.30	0.13	**0.77**	**0.78**	**0.48**
Milk composition, %							
Fat	3.51	3.49	3.48	0.15	**0.90**	**0.83**	**0.66**
Protein	2.97	2.95	2.96	0.07	**0.80**	**0.52**	**0.69**
DMI, lbs/d	71.7	69.1	70.2	2.0	**0.40**	**0.18**	**0.44**
Feed Efficiency	1.54	1.58	1.57	0.05	**0.43**	**0.21**	**0.37**

- **Also no difference in milk FA profile**

Daily Pattern of Feed Intake



➢ ANOVA

Effect	*P*-value
Treatment	0.78
Time	<0.01
Treatment x Time	<0.01

➢ Circadian Parameters

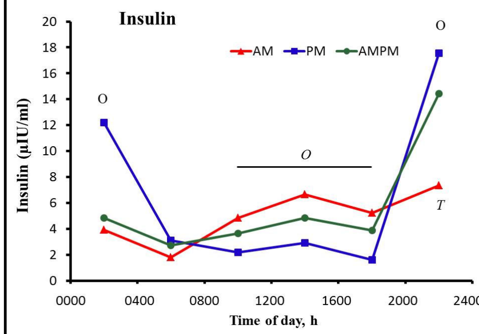
Treatment	Phase/h	Amplitude	*P*-value
AM	1654	2.0	<0.01
PM	1638*	0.6*	<0.01
AMPM	1448*	1.1*	<0.01

*Significantly ($P < 0.05$) different from AM

❖AM vs.PM (O = $P < 0.01$, and *O* = $P < 0.05$); AM vs. AMPM (T $P < 0.01$, and *T* $P < 0.05$)

- Conditional meals were larger at the evening feeding
- Modestly higher intake rate in the early afternoon for **AM**

Daily Rhythm of Plasma Insulin



➢ ANOVA

Effect	*P*-value
Treatment	0.76
Time	<0.01
Treatment x Time	<0.01

➢ Circadian Parameters

Treatment	Phase/h	Amplitude	*P*-value
AM	1844	1.8	0.07
PM	0031*	8.3*	<0.01
AMPM	2220*	4.8*	<0.01

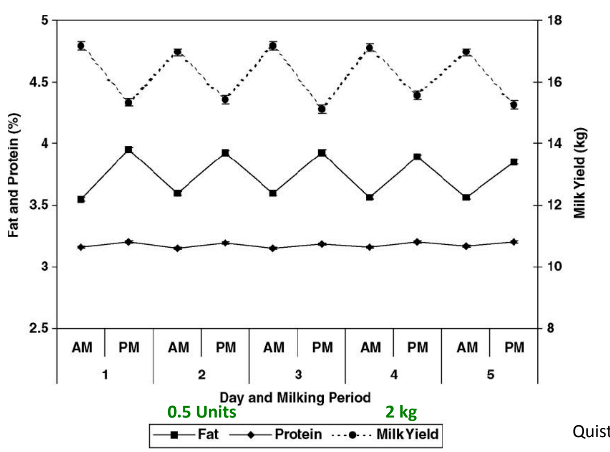
*Significantly ($P < 0.05$) different from AM

❖AM vs.PM (O = $P < 0.01$, and *O* = $P < 0.05$); AM vs. AMPM (T $P < 0.01$, and *T* $P < 0.05$)

- Fresh feed delivery at night resulted in greater insulin secretion
- Morning feeding moderately increased insulin in the early afternoon

Milk Synthesis is Variable Over the Day

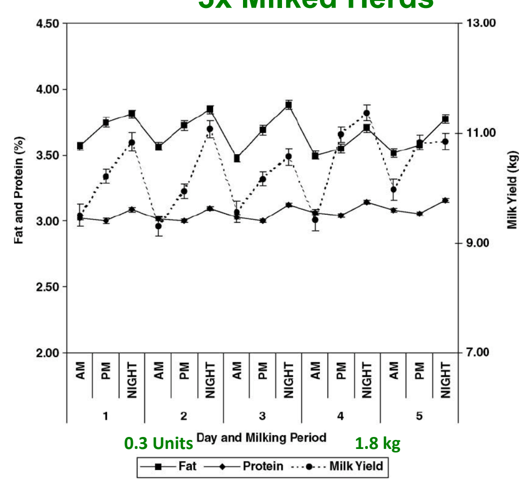
2x Milked Herds



Quist et al. 2008

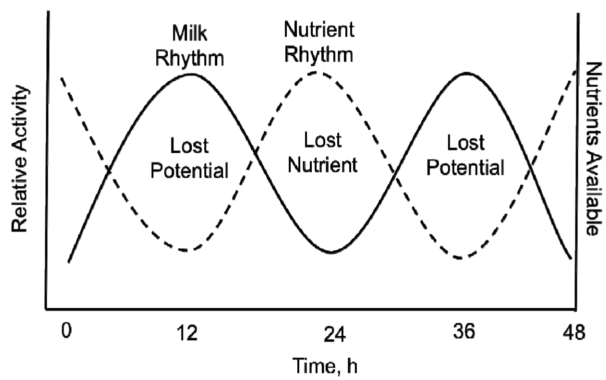
Milk Yield is Variable Over the Day

3x Milked Herds



Quist et al. 2008

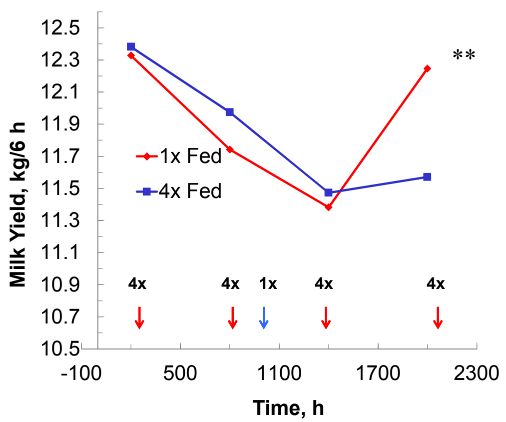
Theoretical De-Synchronization of Intake and Mammary Metabolism



Interaction of Intake and Milk Synthesis

- **Hypothesis**
  - The dairy cow has a circadian rhythm of milk synthesis that is dependent on the timing of nutrient absorption
- **Fed cows 1 x/d or 4 x/d in equal meals**
- **Milked 4 x/d**

Milk Yield, kg/milking



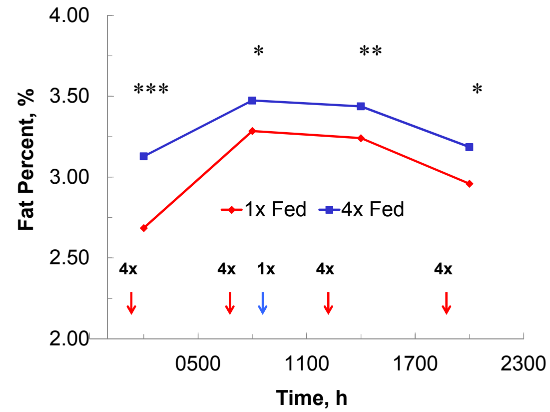
Effect	*P*
Trt	0.64
Time	<0.001
Trt*Time	0.05

Trt	MY, kg/d
1x Fed	47.3
4x Fed	47.1
SEM	0.64

** P< 0.01

Rottman et al. 2014

Milk Fat Percent, %



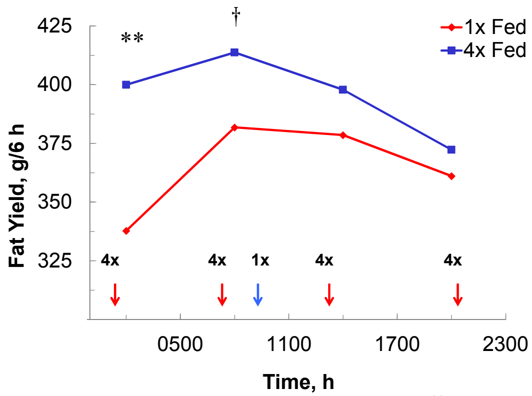
Effect	*P*
Trt	<0.001
Time	<0.001
Trt*Time	<0.05

Trt	Daily AVG Fat %
1x Fed	3.09
4x Fed	3.35
SEM	0.15

* P< 0.05; ** P< 0.01; *** P< 0.001

Rottman et al. 2014

Milk Fat Yield, g/milking



Effect	Pr > F
Trt	<0.001
Time	<0.01
Trt*Time	0.05

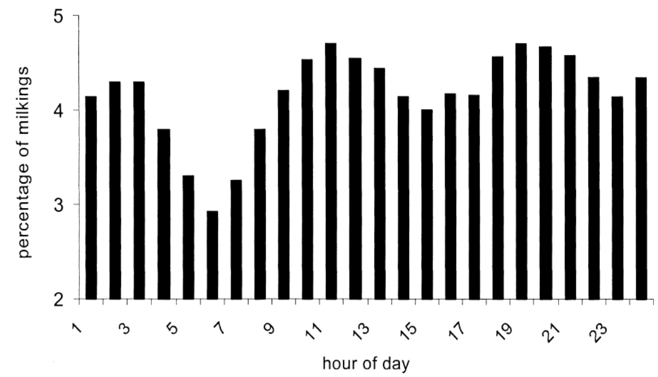
Trt	Fat, g/d
1x Fed	1465
4x Fed	1592
SEM	90

** P< 0.01; † P< 0.1

Rottman et al. 2014

When do cows prefer to be milked??

Automated Milking System



Hogeveen et al., 2001

How Can We Use This Information??

"Circadian Feeding Strategies"

Match the timing of delivery and diet composition to the temporal requirements of the rumen and the cow

1st… Think of the rumen

- Can we stabilize the amount of fermentable organic matter entering the rumen over the day?
- Feeding a single TMR does not provide this since there is high and low periods of intake over the day

Feeding Multiple TMRs over the Day

- **Three diets were used**
  - Control (Con): 30.1% NDF
  - High fiber (H): 31.8% NDF
  - Low fiber (L): 26.9% NDF

70% of H & 30% of L = Control

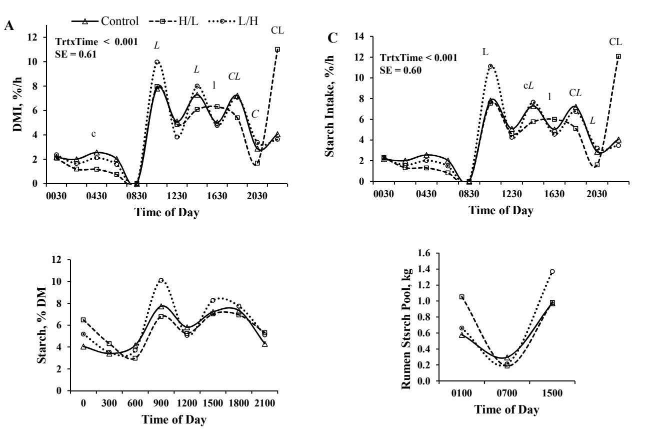
- **Three Treatments**
  - **Fed control TMR once per day at 0900**
  - **High-Low Treatment (HL)**
    - 70% of feed fed as High Fiber Diet at 0900 h
    - 30% of feed fed as Low Fiber Diet at 2200 h
  - **Low-High Treatment (LH)**
    - 30% of feed fed as Low Fiber Diet at 0900 h
    - 70% of feed fed as High Fiber Diet at 1300 h

Rottman et al. 2015; Ying et al. 2015

Milk Yield and Composition

	Treatment				*P*-value
	CON	**HL**	**LH**	**SEM**	**Trt**
DMI, lbs/d	58.0	53.7[c]	56.0	2.4	0.01
Milk, lbs/d	87.3	84.9	90.2	5.3	0.14
Milk Fat					
Percent	3.44	3.39	3.45	0.25	0.73
Yield, lbs/d	2.99	2.82[LH]	3.10	0.11	0.07
Milk Protein					
Percent	3.08	3.10	3.10	0.09	0.86
Yield, lbs/d	2.68	2.64	2.79	0.15	0.19

Pattern of Intake and Rumen Digesta Composition



Rumen Observations

- **No Change in**
  - **Average pH or time under pH 5.8 or 5.6**
  - **No change in daily average rumen VFA's**
  - **No change in DM or OM digestibility**

What Did We Learn?

- **Its complicated!**
- **Have to be very careful with the effect of timing of feed delivery changing feeding behavior**
- **Demonstrates we don't have to have the same TMR across the day and there are times that feeding different diets might be advantageous**

Summary of Circadian Feeding Strategies

- Feed delivery is a strong signal for feeding which can be used to increase intake during low intake periods of the day
- Make sure feed is available when return from parlor………, but
  - Delivery of feed 2-3 h before or after milking may spread intake more across the day??

Is he crazy or can "Circadian Feeding" concepts be applied in the field?

- **Some products may be most effective during a certain time of day (Both ruminally and post-ruminally)**
- **Multiple rations may not be that more complex**
  - **Feed same ration to entire herd in morning**
  - **Return to "top-off" high groups**

Interesting Call From the Field

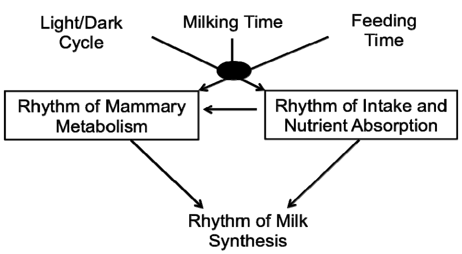
- One pen of cows on a large farm consistently 0.3 to 0.5 units lower in milk fat than peer pen in another barn fed same diet
- Moved fifteen cows from the pen to another pen and they increased milk fat
- Normal MFD troubleshooting turned up no clues
- Cows being fed later in the day (11:30 AM)
- Switched milking and feeding order so feed delivered earlier and before milking.
- Milk fat increased equal to peer pen

Herd Management Associations

- Herds feeding 2x/d had 3.1 lbs higher DMI and 4.4 lb higher milk yield
  - Sova et al. 2013
- Increasing feeding frequency increased number of meals at high stocking rates
  - Crossley et al. 2018
- High milk de novo fatty acid herds were five time more likely to feed more than once per day
  - Woolpert et al. 2017

Summary: Spreading intake across the day is probably better for the rumen and milk yield

- Timing and frequency of feeding and milking most important. Smaller effect of pushing up feed.
- Watch the cows to see how things work on that farm.
- Don't be afraid of different rations across the day!



Lab Members:

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Previous Lab Members:

Dr. Daniel Rico, Dr. Michel Baldin, L. Whitney Rottman, Mutian Niu, Dr. Natalie Urrutia, Richie Shepardson, Andrew Clark, Dr. Liying Ma, and Jackie Ying

USDA United States Department of Agriculture

National Institute of Food and Agriculture

Disclosures

K.J. Harvatine's research in the past 10 years were partially supported by the Agriculture and Food Research Initiative Competitive Grant No. 2010-65206-20723, 2015-67015-23358, 2016-68008-25025 from the USDA National Institute of Food and Agriculture [PI Harvatine], USDA Special Grant 2009-34281-20116 [PI Harvatine], Berg-Schmidt, Elanco Animal Health, BASF, Novus International, PA Soybean Board, Phode Laboratories, Kemin International, Milk Specialties Global, Adisseo, Micronutrients Inc., Organix Recylcing, Insta-Pro Intl., and Penn State University. Harvatine has consulted for Milk Specialties Global, a manufacturer of prilled saturated fat supplements and Micronutrients Inc. as a member of their science advisory boards. Harvatine has also received speaking honorariums from Elanco Animal Health, Novus International, Cargill, Virtus Nutrition, Chr Hansen, NDS, Nutreco, Mycogen, and Milk Specialties Global in the past three years.

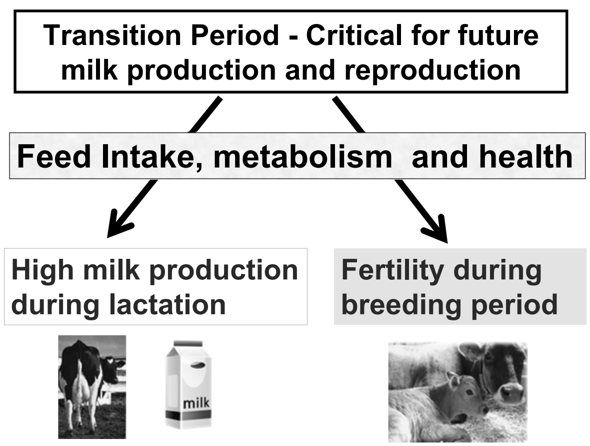
Thank You

Nutrition and Reproduction in Transition Cows

Ron Butler, Cornell University

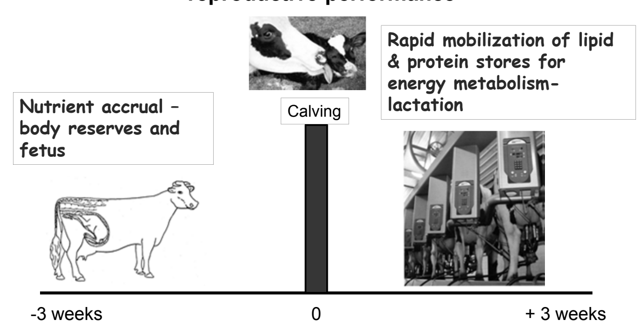
Overview- important concepts:

1) The transition from late pregnancy to the onset of lactation is the most challenging period in the life of a dairy cow – <u>metabolically, health-wise, and nutritionally.</u>
2) The interaction of these factors sets the tone for each cows' milk production and reproductive success during lactation.
3) We will explore how the interaction of feed intake, energy metabolism and health status during the transition period can exert carry-over effects on reproductive performance of cows.

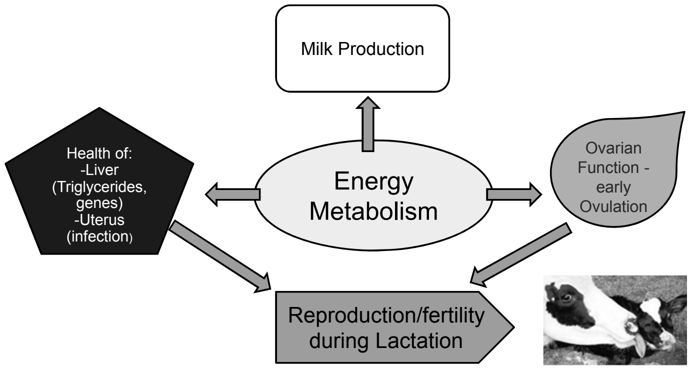


Periparturient transition period

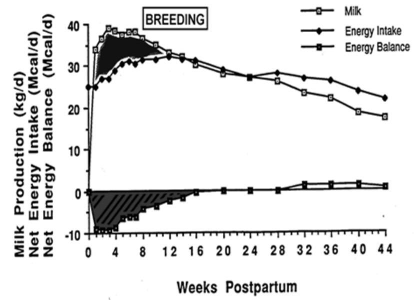
Cascade of metabolic and physiological changes important for milk production, health and future reproductive performance



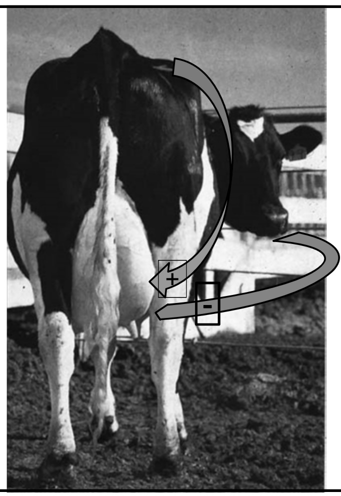
The importance of energy metabolism in the lactating dairy cow



Negative energy balance in early lactation- energy intake lags requirements



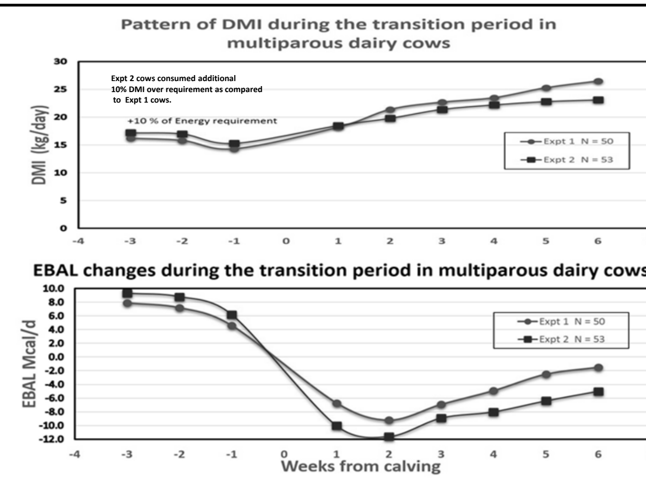
NEBAL during transition period results in marked shifts in metabolic hormones (insulin, IGF-I, GH) and metabolites (low glucose; ↑ NEFA & BHBA)



Negative Energy Balance - NEBAL

Feed energy intake is less than the energy required for milk production plus maintenance and the balance is mobilized from reserves of body fat.

Differences in NEBAL between cows at the same stage of lactation are **most related to differences in DMI.**



Why is DMI already lower for some cows 4 weeks before calving??

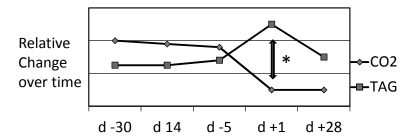
Far-off dry period energy supply carries over and affects metabolism in close-up period:

a. ↑ NEFA
b. ↑ oxidative stress in liver → ↓ DMI

Overfeeding energy during the far-off dry period has a greater carry-over effect on peripartum metabolism than differences in close-up period.

-During first 10 DIM, cows fed 80-100% NRC had ↑DMI, ↑EBAL, ↓NEFA & BHBA compared to 150%. #4563

Excessive energy intake (150%) during far-off period ↓ liver oxidation of NEFA to CO_2 (by 20%) and ↑ esterification (1.8X) to triacylglycerol (TAG)*. #3764



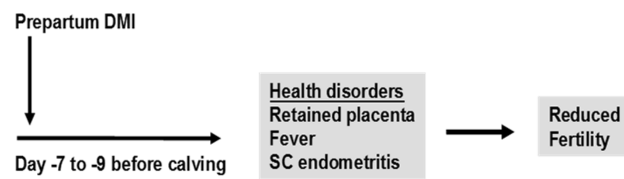
Dietary strategies during the dry period to reduce NEBAL

- Goal – meet, but do not exceed energy requirements by more than10-20% in far-off or close-up dry period.
- Control energy intake via high-bulk diets (straw):
  ~1.3 Mcal NEL/kg DM = ~15 Mcal/d/cow. Must meet requirements for protein, minerals & vitamins.

Or

- Limit feeding of higher energy diet.
  - Limit feeding difficult to manage successfully when heifers and cows are co-mingled in pens with social and behavioral interactions.

Prepartum DMI and Health



- **1-2 weeks pre-calving**
  - **Following fresh feed**
  - **⇓ Time eating**
  - **⇓ DMI**

1 kg ⇓ = 3X risk for metritis

➢**Social behavior and interactions affects transition cow health**

Prepartum decreases in DMI and energy balance are associated with postpartum health problems that impact fertility

- 1-2 weeks prepartum, cows that will develop uterine disease had ↓ DMI, ↑ NEFA, and ↓ neutrophil function.
- Prepartum NEFA provides monitoring tool for risks of RP, metritis and reduced pregnancy rate during lactation.
- ↑ NEFA during transition is associated with signs of **<u>liver inflammation</u>**, perhaps **via oxidative stress**, that may promote metabolic disorders.
- **Uterine inflammation** at calving is exacerbated by **NEBAL** and alters uterine involution ie. subclinical endometritis → delayed Ov and pregnancy.

Detrimental effects of NEFA and BHB during transition on future reproductive performance

Higher prepartum NEFA & BHBA → ↑ RP and other diseases. Qu, Y., A. N. Fadden, M. G. Traber, and G. Bobe. Potential risk indicators of retained placenta and other diseases in multiparous cows. J Dairy Sci 97 (7):4151-4165, 2014.

↑ NEFA & ↑ BHBA during transition period:

→ 13-20 % **decrease in risk of pregnancy during breeding**.

Large field study with 91 herds & 2250+ cows. Ospina, P. A., D. V. Nydam, T. Stokol, and T. R. Overton. Associations of elevated nonesterified fatty acids and beta-hydroxybutyrate concentrations with early lactation reproductive performance and milk production in transition dairy cattle in the northeastern United States. J.Dairy Sci. 93 (4):1596-1603, 2010.

→ 1.9X ↑ risk of metritis, 1.7X risk of RP, ↓ risk of pregnancy 1st AI, 23% ↑ time to pregnancy. Meta-analysis. Abdelli, A., D. Raboisson, R. Kaidi, B. Ibrahim, A. Kalem, and M. Iguer-Ouada. Elevated non-esterified fatty acid and beta-hydroxybutyrate in transition dairy cows and their association with reproductive performance and disorders: A meta-analysis. Theriogenology 93:99-104, 2017.

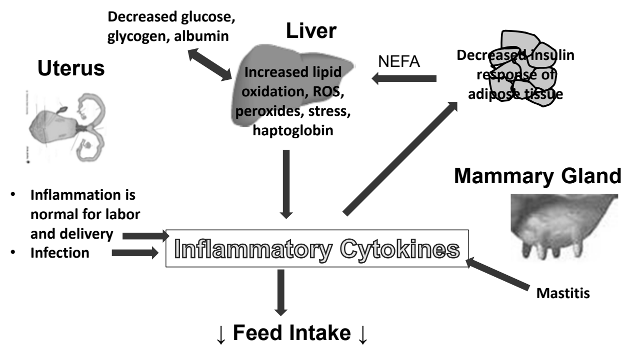
Prepartum decreases in DMI and energy balance are associated with postpartum health problems that impact fertility

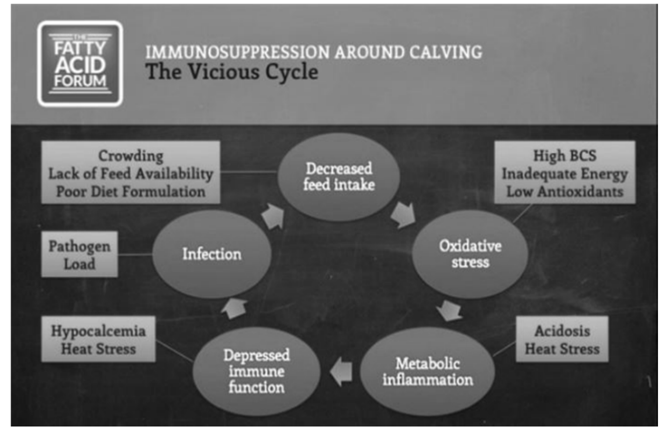
- 1-2 weeks prepartum, cows that will develop uterine disease had ↓ DMI, ↑ NEFA, and ↓ neutrophil function.
- Prepartum NEFA provides monitoring tool for risks of RP, metritis and reduced pregnancy rate during lactation.
- ↑ NEFA during transition is associated with signs of **<u>liver inflammation</u>**, perhaps **via oxidative stress**, that may promote metabolic disorders.
- **Uterine inflammation** at calving is exacerbated by **NEBAL** and alters uterine involution ie. subclinical endometritis → delayed Ov and pregnancy.

Liver metabolism during transition period

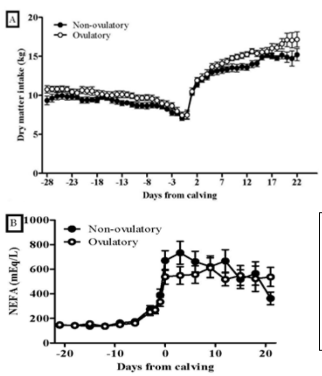
- Liver adaptation to increased availability of NEFA is increased lipid oxidation for energy.
- First step produces reactive oxygen species (ROS) that can form lipid peroxide.
- **Perhaps via oxidative stress, peroxides can trigger <u>liver inflammation</u>**, decreased DMI and shifts in liver metabolism of carbohydrates and lipids that may lead to metabolic disorders.
- Healthy liver – increased glucose (gluconeogenesis), glycogen and albumin (-APP).
  - – with inflammation, decreases in these, increased +APP and accumulation of triglycerides.

Inflammation is common in transition cows





Peripartum changes in DMI associated with reproductive performance

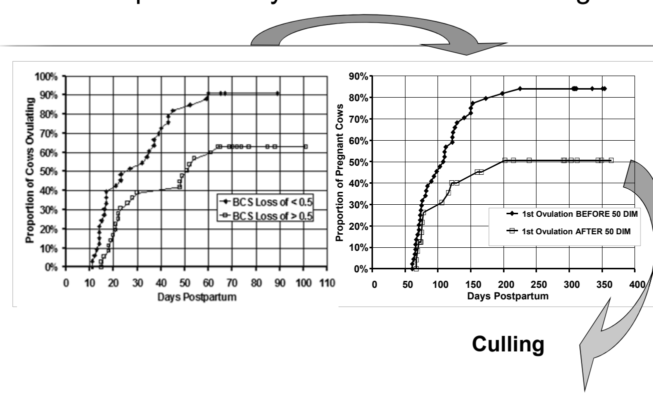


As early as 4 weeks prepartum, differences in DMI and NEBAL (↑NEFA) are apparent in cows that develop OV *vs.* NOV follicles during first 3 weeks postpartum.

Why is this important??

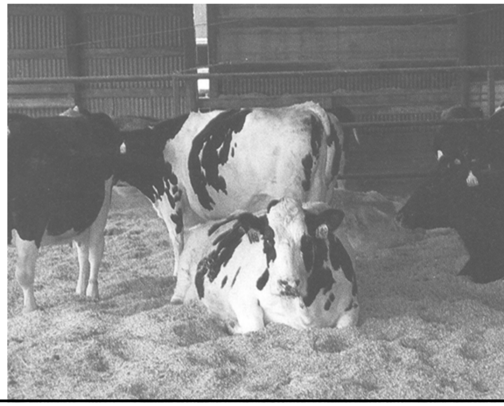
Early ovulation during lactation is associated with higher fertility later during the breeding period.
→ ↑ uterine environment (progesterone**)**
- associated ↑ metabolic signals (IGF-I)

Early NEBAL & BCS loss delays first ovulation and relates to poor fertility/increased risk of culling



Culling

Metabolic effects on ovarian follicular development begin during the dry period!

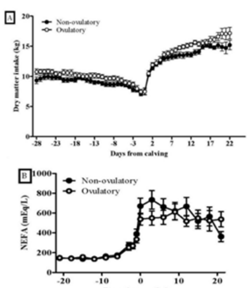


Prepartum differences in dry matter intake (DMI), energy balance and metabolic hormones are associated with **postpartum follicle outcome**

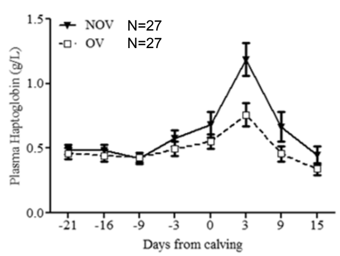
- Not surprising, if we consider that full follicular development requires many weeks (60-80 days) for completion *ie.* does not just begin after calving.

Peripartum changes in DMI associated with reproductive performance

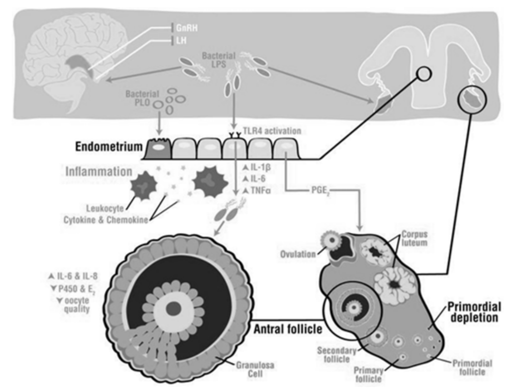
↓ DMI ↑NEBAL/NEFA



Hepatic acute phase response – Haptoglobin
- Ovulatory vs. Nonovulatory follicles



Uterine infection links with infertility in dairy cows



Bromfield et al., 2015 JAS 93:2021-2033

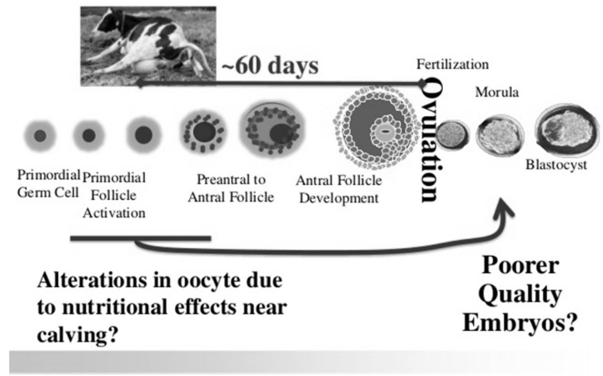
From calving to breeding, both uterine disease/inflammation or non-uterine diseases/inflammation reduce fertility after insemination

- Uterine disease/inflammation affects both developing oocytes in ovarian follicles and the uterine environment -- site of embryo development.
- Non-Ut disease at either preantral or antral follicle stage → ↓ pregnancy rate.
  -suggests reduced oocyte competence as the most likely effect.

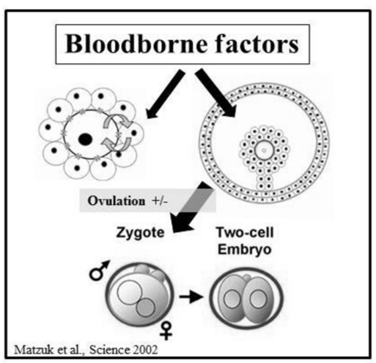
UT Disease = Ret. Placenta & metritis
NUT Disease = Mastitis, lameness, digestive & respiratory diseases

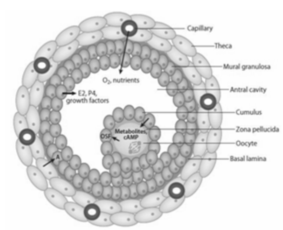
E. S. Ribeiro, A. P. A. Monteiro, R. S. Bisinotto, F. S. Lima, L. F. Greco, A. D. Ealy, W. W. Thatcher, and J. E. P. Santos. Conceptus development and transcriptome at preimplantation stages in lactating dairy cows of distinct genetic groups and estrous cyclic statuses. *J Dairy Sci 99 (6):4761-4777, 2016.*

Potential Causes of Early Embryo Degeneration



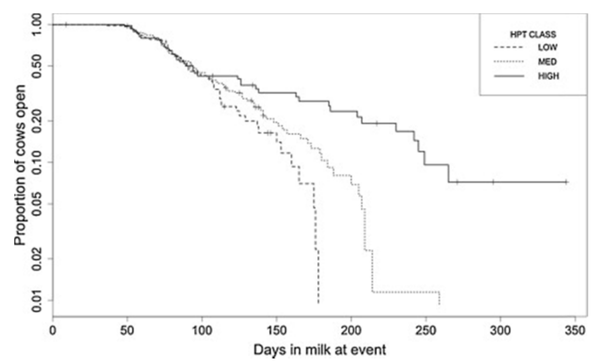
Blood born factors related to inflammation can transfer into follicular fluid to affect oocyte growth and viability, ovulation and embryo survival





Krisher, R.L. Ann. Rev. Anim. Biosci. 1:393, 2013

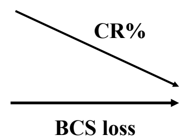
Survival curves for days to conception associated with plasma concentrations of haptoglobin (low, medium or high) following calving (d 2-8) in clinically healthy multiparous dairy cows (n=240)



Relationships between negative energy balance (NEBAL), body condition score (BCS) and conception rate (CR) to first insemination in high producing dairy cows

High milk production and NEBAL results in tissue mobilization and BCS loss.

Greater BCS loss during early lactation lowers fertility to insemination



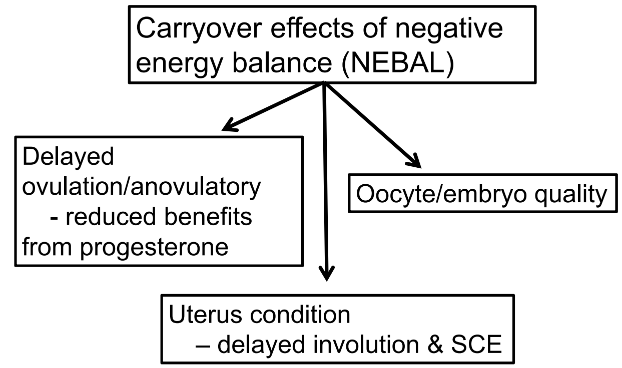
BCS change from calving to AI (70 DIM; 6400 cows)

	Pregnancy %	Odds Ratio	Pregnancy loss, %
≥ 1 unit	28	Referent	20.5
< 1 unit	37	1.4	14.5
No Change	42	1.7	10.7

Santos et al., An.Reprod.Sci. 110:207, 2009

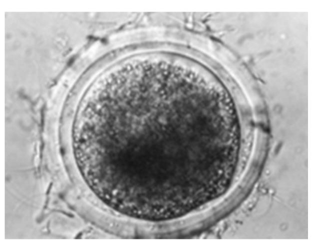
CR % among quartiles milk yield to 90 DIM – *NS*

Low fertility to AI in lactating dairy cows

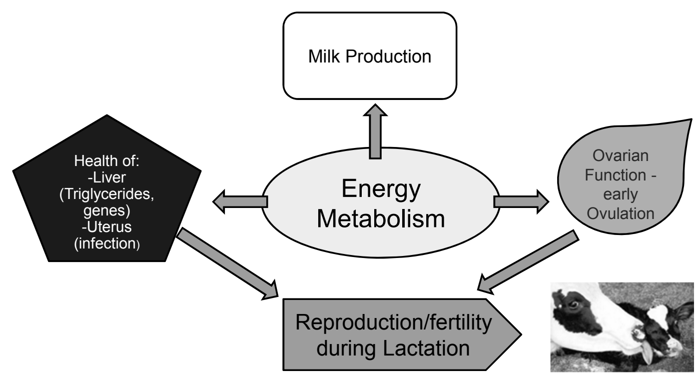


Effects of energy metabolism and/or inflammation on fertility to insemination

Oocyte health and embryo quality



The importance of energy metabolism in the lactating dairy cow



Take Home Message- 1

- Metabolic changes in periparturient cows associated with the onset of **negative energy balance** appear most responsible for the detrimental effects on both health and reproductive performance.
- Negative energy balance related to decreased **DMI** during early lactation is the **major nutritional link to low fertility** in lactating dairy cows.
- Negative energy balance delays recovery of postpartum reproductive function and exerts carryover effects (BCS, oocytes, uterus) that reduce fertility during the breeding period.

2 - What Nutritional Strategies Benefit Reproductive Performance in cows?

- Dry period feeding – Limit dietary energy intake throughout to maintain moderate BCS (~3.0) at calving; At requirement level.
- Advantages or Benefits:
  - **To minimize ↓ DMI prior to and at calving**
  - To minimize ↑ NEFA pre- and postpartum
  - To minimize negative effects on liver metabolism of NEFA – ↓ metabolic inflammation
  - To facilitate ↑ glucose production by liver for ↑ milk production
  - To minimize ↓ immune function that ↑ risk of infection/inflammation
- Dietary strategies prepartum to minimize hypocalcemia postpartum.
  - Feed low calcium diet
  - Feed anionic salts to optimize DCAD ratio
- What about feeding fat supplements??

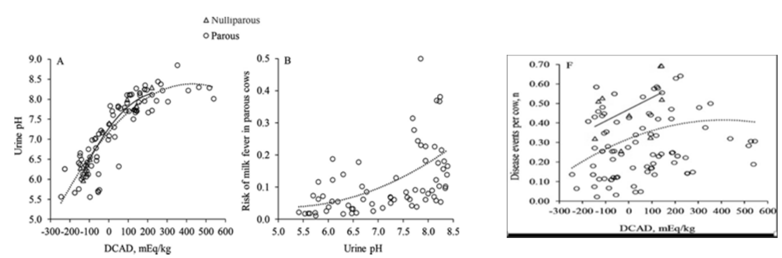
Effects of dietary fat or fatty acids on fertility in dairy cattle

- Overall, including fats in transition diets improves fertility: pregnancy to insemination ↑ 27% & calving to pregnancy interval ↓16%. Limited number of studies precludes pinpointing specific fatty acids. Rodney, R. M., P. Celi, W. Scott, K. Breinhild, and I. J. Lean. Effects of dietary fat on fertility of dairy cattle: A meta-analysis and meta-regression. J Dairy Sci. 98 (8):5601-5620, 2015.
  - Many studies have shown mixed effects and raise a general concern – high lipid load from late pregnancy until calving, no matter if stored, mobilized or fed, affects the endocrine system, metabolism and ↓ DMI → ↑ risk for metabolic disorders PP. B. Kuhla, C. C. Metges, and H. M. Hammon. Endogenous and dietary lipids influencing feed intake and energy metabolism of periparturient dairy cows. Domest.Anim Endocrinol. 56 Suppl:S2-S10, 2016.
- Feeding n-3 Fatty Acids PP: fish oil (Ca salts > 30 DIM) or rumen-protected n-3 FA (0-60 DIM) → ↓ pregnancy losses after AI to → ↑ % pregnant. Silvestre, F.T., T. S. Carvalho, N. Francisco, J. E. Santos, C. R. Staples, T. C. Jenkins, and W. W. Thatcher. Effects of differential supplementation of fatty acids during the peripartum and breeding periods of Holstein cows: I. Uterine and metabolic responses, reproduction, and lactation. J Dairy Sci. 94 (1):189-204, 2011;
- S. Elis, S. Freret, A. Desmarchais, V. Maillard, J. Cognie, E. Briant, J. L. Touze, M. Dupont, P. Faverdin, V. Chajes, S. Uzbekova, P. Monget, and J. Dupont. Effect of a long chain n-3 PUFA-enriched diet on production and reproduction variables in Holstein dairy cows. Anim Reprod.Sci. 164:121-132, 2016.
- CLA

Meta-analysis of the effects of prepartum dietary cation-anion difference on performance and health of dairy cows - DCAD

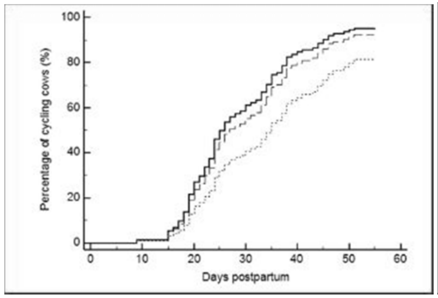
J.E.P. Santos, I.J. Lean, H. Golder, E. Block J Dairy Sci DOI: 10.3168/jds.2018-14628 Results from 42 Experiments

Feeding negative DCAD diet prepartum benefits Milk Production and DMI Postpartum and reduces disease events (RP, Metritis, DA and Milk Fever)



Lower Disease Events and Inflammation ⇨ Improved Fertility during Breeding Period

L. S. Caixeta, P. A. Ospina, M. B. Capel, and D. V. Nydam. Association between subclinical hypocalcemia in the first 3 days of lactation and reproductive performance of dairy cows. *Theriogenology 94:1-7, 2017.* *Used 97 cows in 2 NY herds*



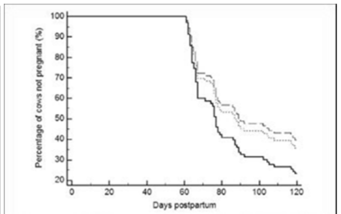


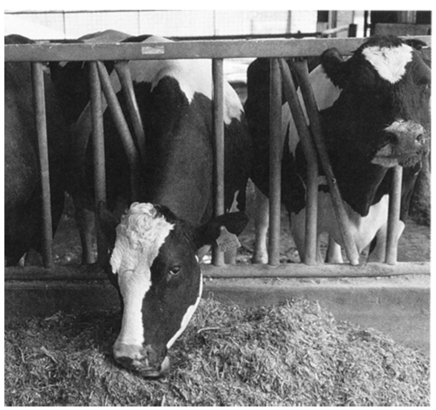
Fig. 3. Cox Proportional-Hazard curves for time to pregnancy in the first 120 DIM for eucalcemic animals (eucalcemia; n = 19; solid line), subclinical hypocalcemia (SCH; n = 45; dashed line) or chronic subclinical hypocalcemia (cSCH; n = 33; dotted line). Compared to the eucalcemic group the hazard ratio for subclinical hypocalcemic cows was 0.63 (95% CI = 0.33–1.23; *P* = 0.2) and 0.71 for chronic SCH (95% CI = 0.36–1.39; *P* = 0.3).

Milk production record-2016 FOCUS on DMI at calving

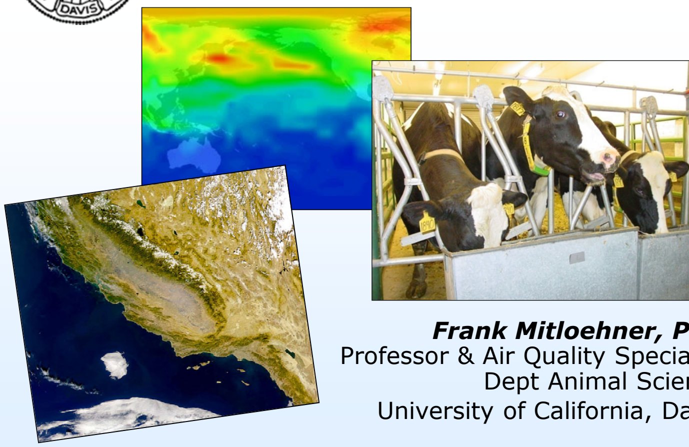
Can you imagine Gigi's feed intake/DMI capability and pattern after calving?? ~Minimum 90 lb DMI/d avg. What is the likelihood Gigi had PP health problems??

- Bur-Wall Buckeye Gigi, produced 74,650 pounds of milk with 2,126 pounds of fat and 2,142 pounds of protein- 365d.
  - 204 lbs milk/d average.
- Gigi achieved this as a nine-year-old, after a 61,000 pound record as an eight-year-old.

Questions???



Livestock and Climate Change: Fact or Faked



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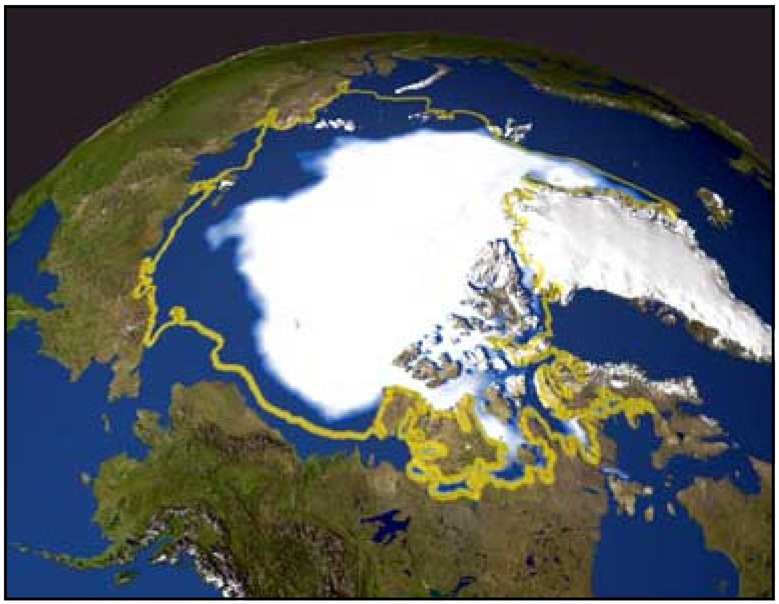
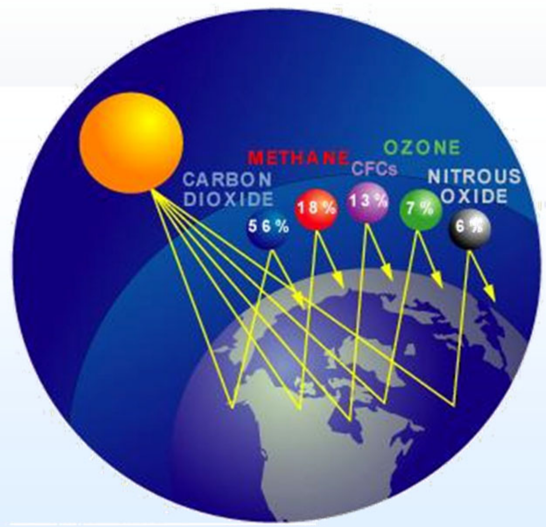
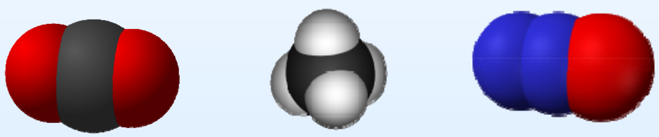




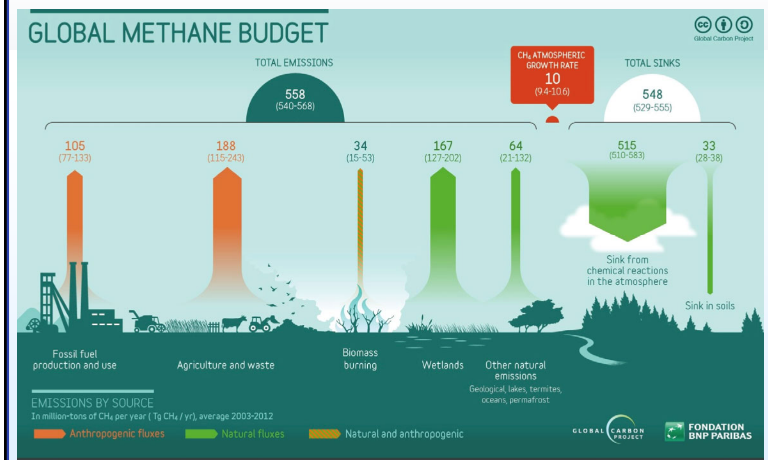
GHG & GWP

Global Warming Potential (GWP) of Main GHG

- Carbon Dioxide, CO_2 1
- Methane, CH_4 28
- Nitrous Oxide, N_2O 298



CO2 – Carbon Dioxide CH4 – Methane N2O – Nitrous Oxide



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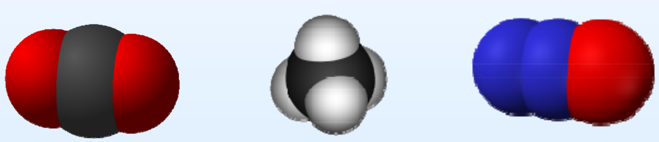
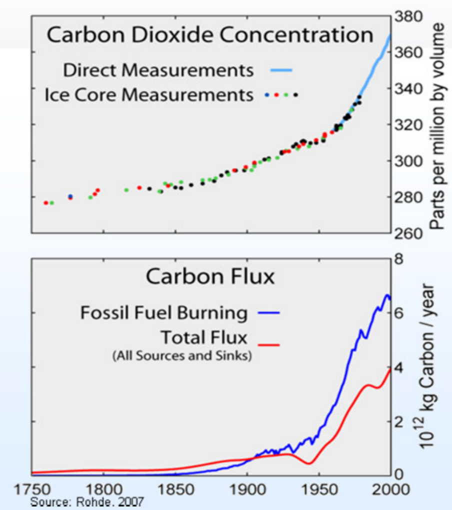


CO2 – Carbon Dioxide CH4 – Methane N2O – Nitrous Oxide

Carbon Dioxide and Carbon Flux



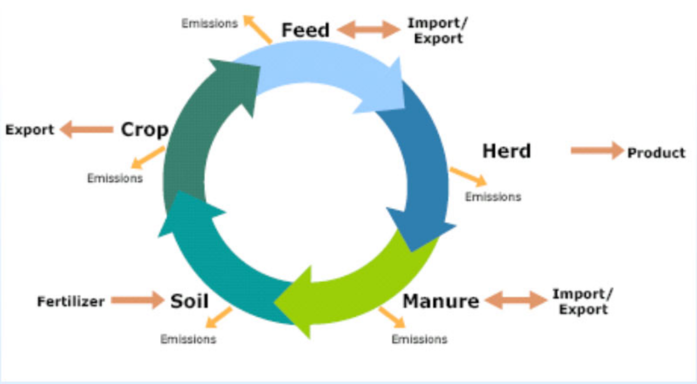
Facts or Fiction on Livestock and Climate Change

- Livestock produces 18% of all anthropogenic GHG globally
- Livestock produces more GHG than transportation
- Livestock occupies 70% of all agricultural land globally
- Grazing systems produce less GHG than conventional animal production in confinement systems

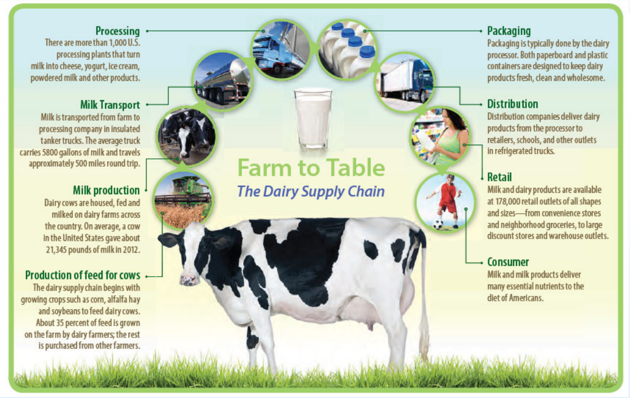
"Livestock's Long Shadow" (FAO, 2006)

- "The Livestock sector is a major player, responsible for 18% of GHG emissions measured in CO_2e. This is a higher share than transport"

Life Cycle Assessment



(NRC, 2003)



BBC Home News Sport Weather TV Radio

Page last updated at 00:15 GMT, Wednesday, 24 March 2010

UN body to look at meat and climate link

By Richard Black
Environment correspondent, BBC News

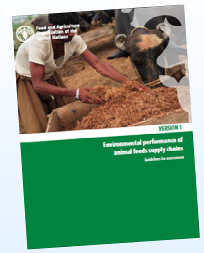
Livestock's Long Shadow calculated meat-related emissions from field to abattoir

UN specialists are to look again at the contribution of meat production to climate change, after claims that an earlier report exaggerated the link.

"I must say honestly that he has a point - we factored in everything for meat emissions, and we didn't do the same thing with transport, we just used the figure from the IPCC."

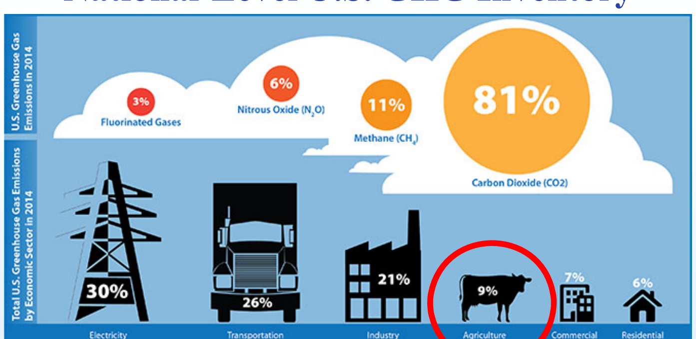
Dr. Pierre Gerber, LLS contributing author

Livestock Environmental Assessment and Performance Partnership (LEAP)



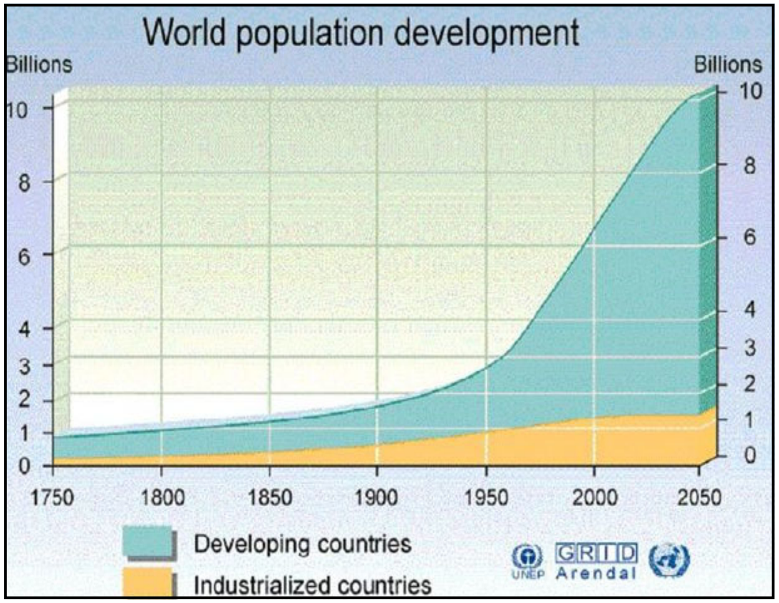
- Internationally agreed sector-level methodologies and guidance to allow
  - transparent,
  - robust,
  - and fair measurement of the environmental performance of livestock supply chains
- FAO / LEAP LCA Guidelines officially released

National-Level U.S. GHG Inventory

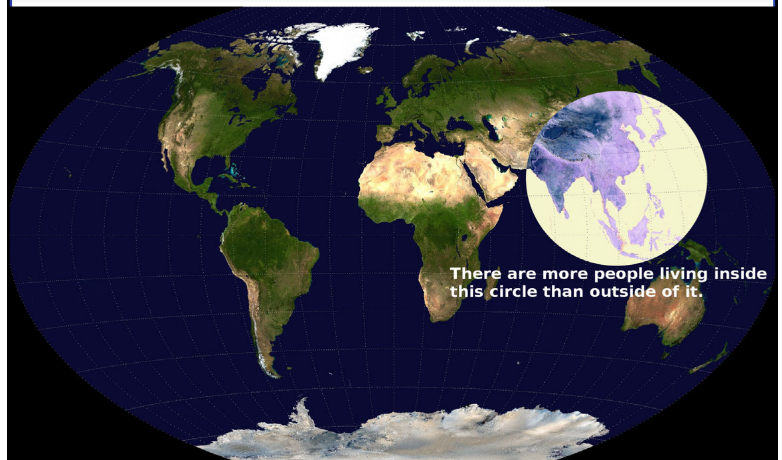


Source: EPA (2016)

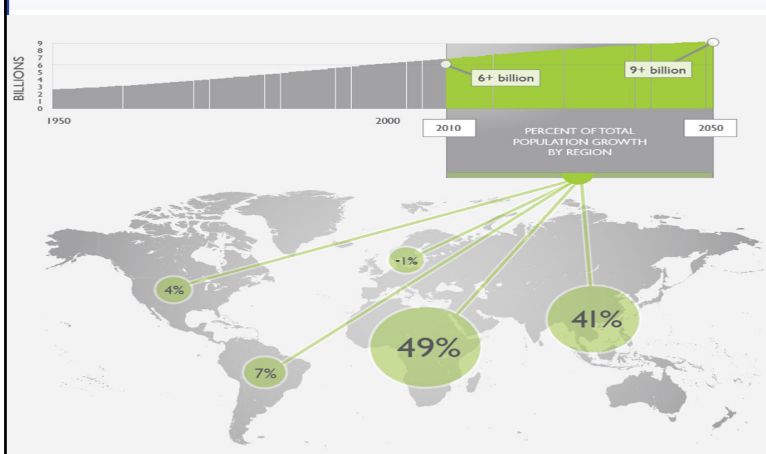
National Geograpic



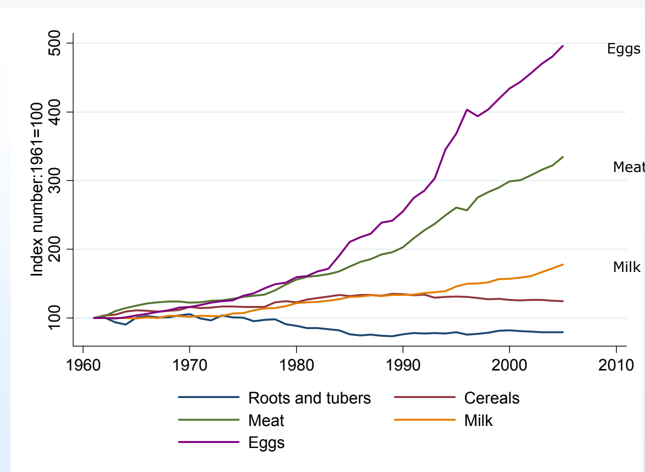
4.5 Billion + population of USA in 10 years



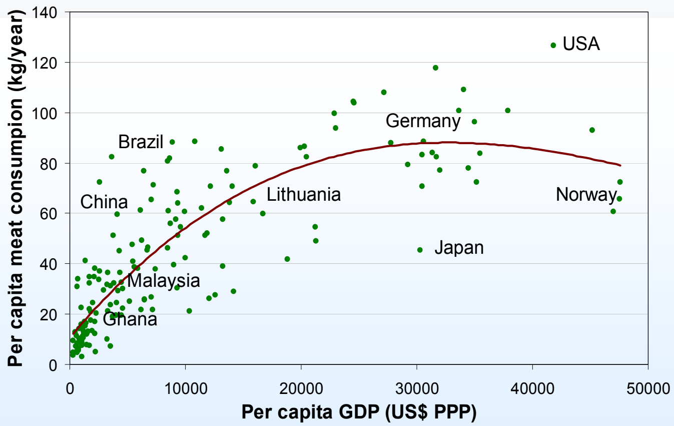
Today and Tomorrow's Markets



Consumption is growing rapidly in developing countries



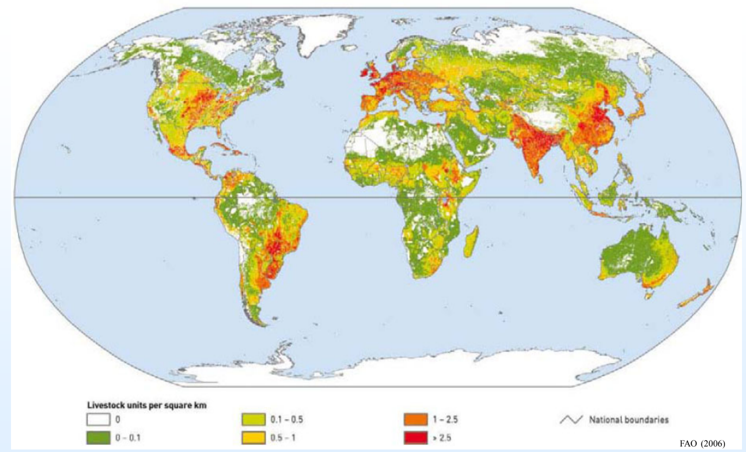
… driven by incomes …



21

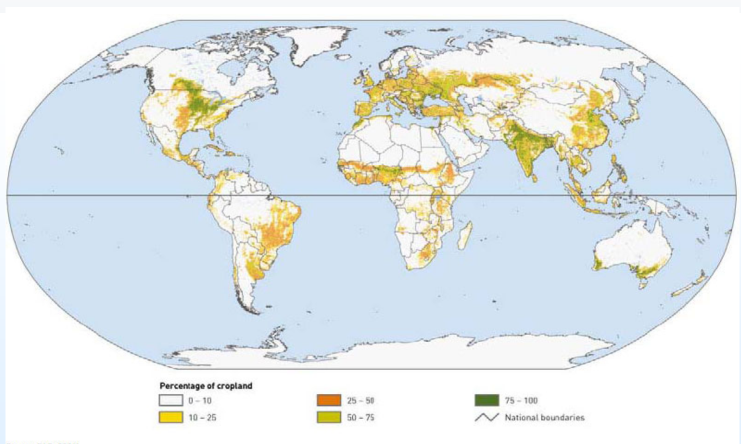
Per capita GDP and meat consumption by country, FAO, 2005.

Global livestock distribution



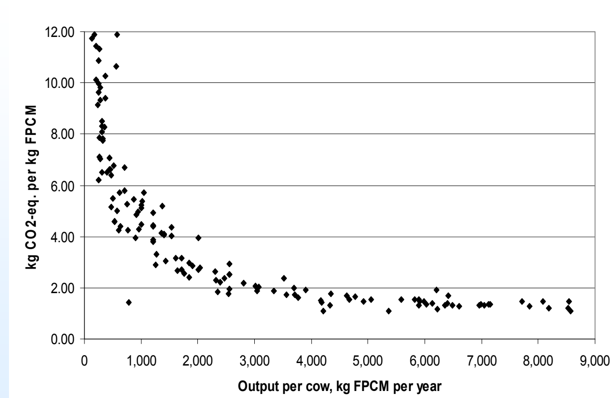
FAO (2006)

Distribution of cropland

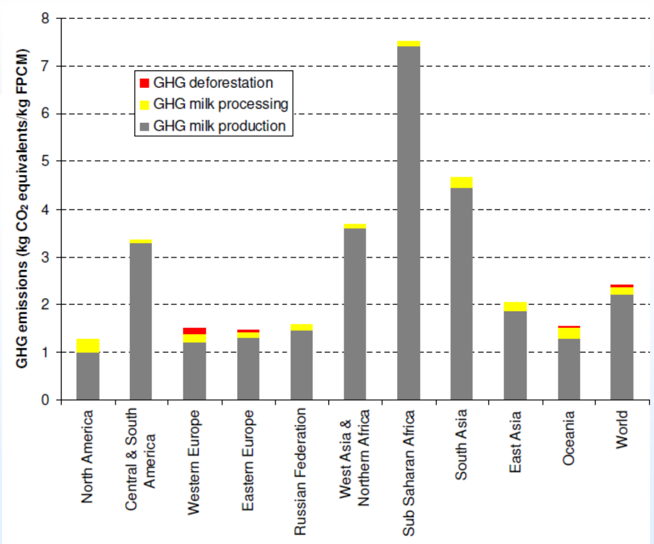


FAO (2006)

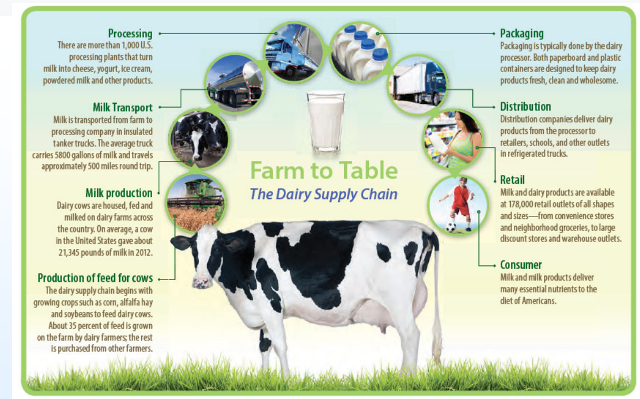
Relationship between total greenhouse gas emissions and milk output per cow



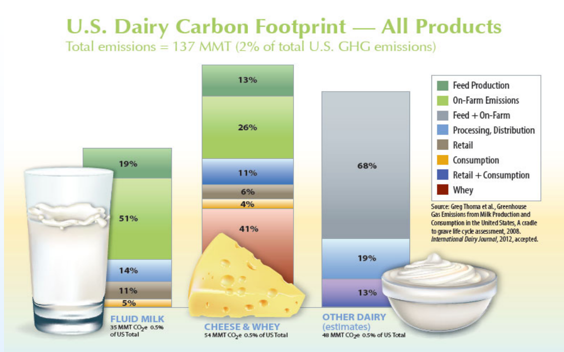
H. Steinfeld, 2015



FAO (2010)

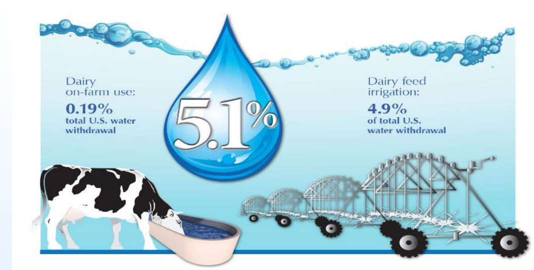


Dairy is ~2% of Total US Greenhouse Gas Emissions



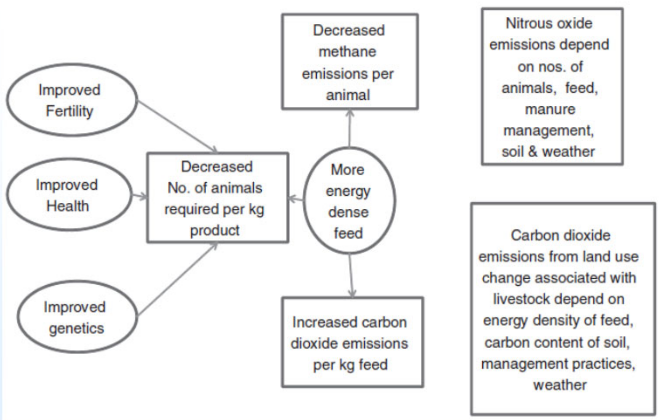
Source: G. Thoma et al. Volume 31, Supplement 1, Pages S1-S100 (April 2013)

Key finding: Dairy uses ~5.1% of U.S. water withdrawal



Henderson, A., Asselin, A., and Heller, M., et al., U.S. Fluid Milk Comprehensive LCA. University of Michigan &University of Arkansas, 2012.

Mitigation: interventions to improve productivity



Gill et al. (2010)

US Dairy trends

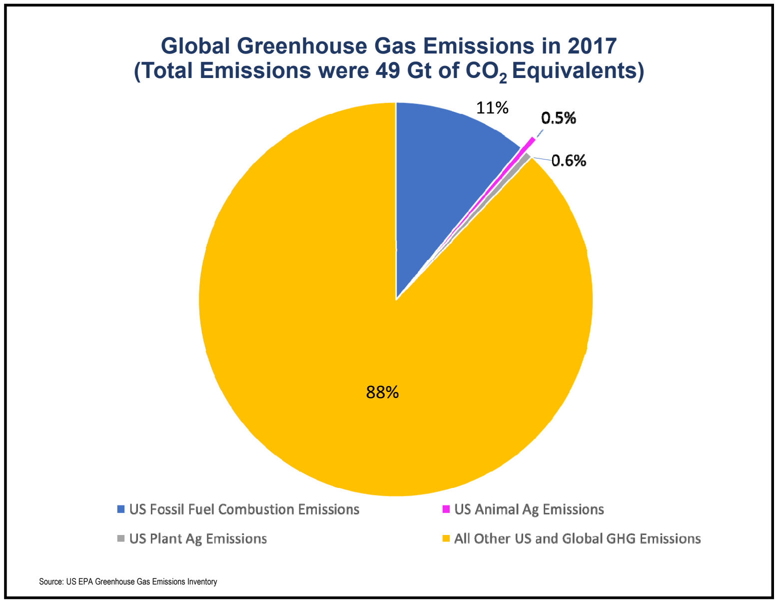
- In 1950, there were 25 million dairy cows in the US, vs 9 million today
- With 16 million fewer cows (1950 vs 2018), milk production nationally has increased 60 percent
- The carbon footprint of a glass of milk is 2/3 smaller today than it was 70 years ago

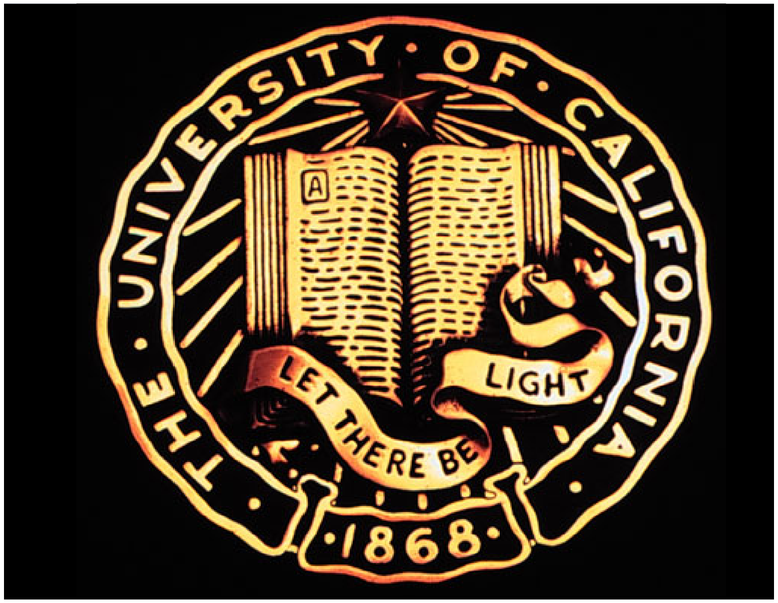
China Swine Example

- China's five year plan focuses on making farms larger and more efficient
- Half of the world's pigs live in China
- 50 million sows w/ 20 piglets born alive
- Equals annual production of 1 Billion pigs
- Pre-weaning mortality causes 400 Million pigs to never make it to the market
- One more pig per sow would mean 1 Million tons of feed saved

Summary

- Livestock in developing countries contribute to 70-80% of global enteric- and waste emissions (IPCC)
- Reductions of enteric- and manure emissions possible
- Production intensity and emission intensity are inversely related


Global Greenhouse Gas Emissions in 2017
(Total Emissions were 49 Gt of CO_2 Equivalents)
11%
0.5%
0.6%
88%
US Fossil Fuel Combustion Emissions
US Animal Ag Emissions
US Plant Ag Emissions
All Other US and Global GHG Emissions
Source: US EPA Greenhouse Gas Emissions Inventory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LET THERE BE LIGHT
1868

Current concepts in hypocalcemia

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9 April 2019

Cornell Dairy Center of Excellence

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Disclosure

This slide informs you that I have received research support from the following corporate entities, some of which also provide compensation for speaking engagements:

- Boehringer Ingelheim Animal Health
- Elanco Animal Health
- Phibro Animal Health

Since the outcomes of my Cornell research may be of interest or may be beneficial to these companies, university policies require that I disclose these potential conflicts. I have disclosed these relationships to Cornell University and they are being managed in accordance with the CU policy 1.7 on financial conflicts of interest related to research.

Overview

- Calcium demands of early lactation
- When is hypocalcemia a problem?
- Postpartum calcium supplementation

The transition period

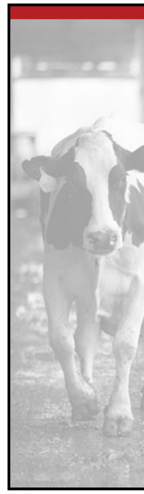
- Time of physical and physiologic change
- 3 weeks before to 3 weeks after calving

colostrum production

uterine involution

3 weeks prepartum

21 days in milk



Calcium demands of milk production

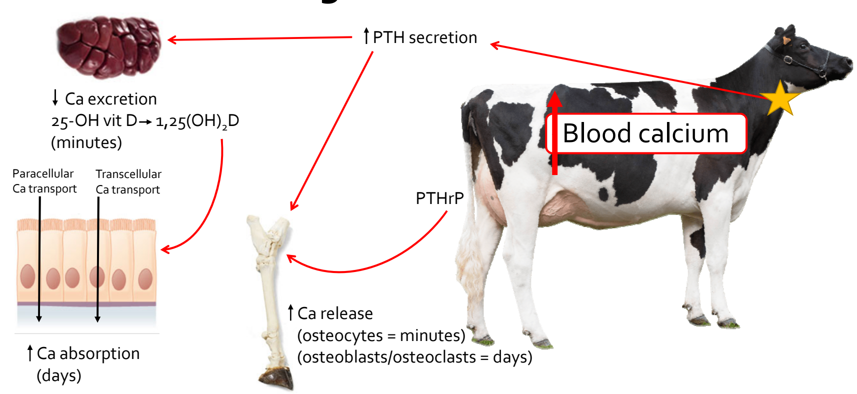
Daily maintenance = 21 g Ca

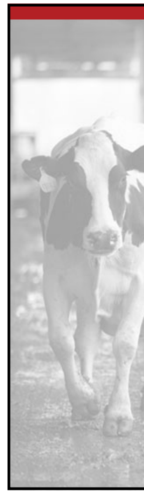
Colostrum = 23 g Ca

100 lb milk = 56 g Ca

- Human recommended dietary allowance = 1,000 mg Ca
- 1 cup milk = 300 mg Ca

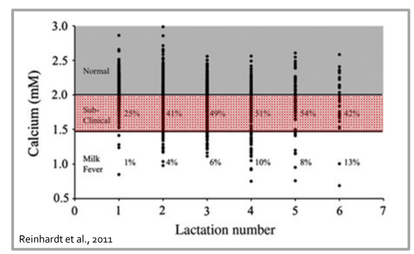
Increasing blood calcium





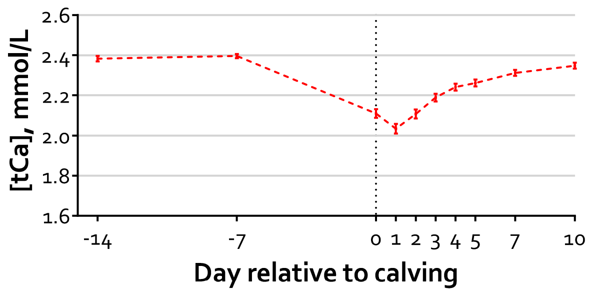
Hypocalcemia

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



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

Periparturient change in blood calcium



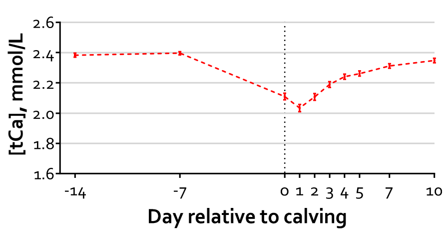
Mean calcium concentration of 407 cows in 2 NY dairy herds.
Bars represent 95% confidence intervals.

Subclinical hypocalcemia (SCH)

- Multiple studies have explored categorization of blood calcium concentrations in early lactation
  Oetzel et al., 1988; Oetzel et al., 1996; Martinez et al., 2012
- Recent studies use epidemiologic outcomes to improve characterization
  Chapinal et al., 2011; Rodriguez et al., 2017; Wilhelm et al., 2017; Neves et al., 2018; Venjakob et al., 2018
- No consensus on optimal test day or what cut point to use for classification of SCH

Is subclinical hypocalcemia bad?

- When to test:
  - At calving?
  - At 24 hrs?
  - At 48 hrs?
  - Later?



- What cut-point to use:
  - Definition of "normal"
  - Based on health and production outcomes

Does calcium concentration at calving matter?

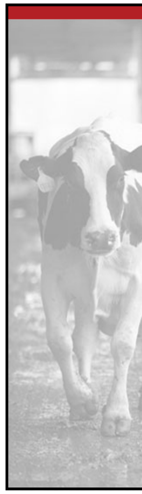
- Prospective cohort study in 5 dairy herds in NY
- 1,416 cows, blood collected by farm employees
- Mean time from calving to blood collection = 3 h

	Farm				
	A	B	C	D	E
Milking cows, n	1,474	567	1,282	1,677	1,222
Milk production, lb	85.5	85.6	81.4	82.1	81.0
Prepartum DCAD, mEq/100 g DM	-6.9	-2.8	-5.5	7.3/14.1	-2.8

Conclusions

tCa: 2.0 mmol/L = 8.0 mg/dL

- Primiparous cows: tCa immediately after parturition was non-informative
- Multiparous cows:
  - Greater tCa increased the risk of culling
    - Every 0.1 mmol/L increase, RR = 3.4 (95% CI = 1.0 to 12.0)
  - Cows with tCa ≤1.95 mmol/L made more milk
    - 94.4 vs. 92.0 lb per test-day ($P < 0.001$)
  - Cows with tCa ≤1.85 mmol/L were more likely to get a DA
    - RR = 2.8 (95%CI = 1.4 to 5.9)



Take-home message (and more questions…)

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

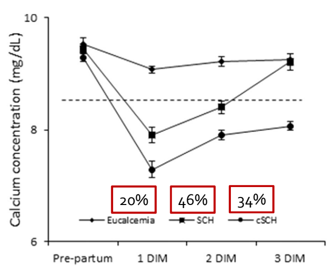
Chronic subclinical hypocalcemia (cSCH)

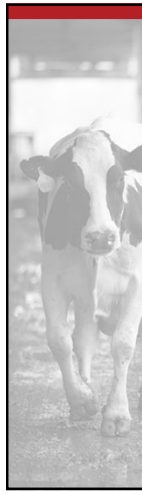
Theriogenology. 2017 May;94:1-7. doi: 10.1016/j.theriogenology.2017.01.039. Epub 2017 Jan 25.

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].

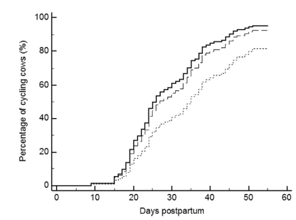
- 2 dairy farms, 97 cows
- Definitions:
  - SCH = serum tCa ≤2.15 mmol/L (8.6 mg/dL)
  - cSCH = SCH at 1, 2, and 3 DIM
- Incidence cSCH:
  - Parity 1 = 20%
  - Parity 2 = 32%
  - Parity ≥3 = 46%





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 ($P = 0.06$)

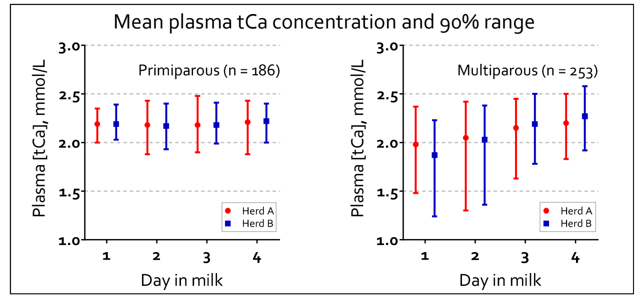


- Pregnancy at first service:
  - cSCH cows had lower odds of pregnancy compared to eucalcemic cows
  - OR = 0.27 ($P = 0.04$)

When does calcium concentration matter?

- Prospective cohort study on 2 dairy herds in NY
  - 396 cows, blood sample collected daily for first 4 DIM
  - Health disorders and daily milk production collected from farm computer records
- Describe temporal association of tCa with:
  - Risk of metritis and/or displaced abomasum
  - Average daily milk yield for first 15 weeks

Descriptive results



Disease	Primiparous, n	Multiparous, n
Metritis	19 (13.9%)	22 (8.5%)
Displaced abomasum	0 (0.0%)	12 (4.6%)

Disease results – primiparous cows

- Reduced tCa at 2, 3, or 4 DIM associated with an increased risk of metritis

DIM	n	*P*-value	AUC	Cut point, mmol/L	% below cut point	RR	95% CI
1	137	0.22	—	—	—	—	—
2	137	0.001	0.78	≤2.15	36.5	4.0	2.0 to 8.0
3	137	<0.001	0.80	≤2.10	26.3	5.2	2.6 to 10.3
4	134	<0.001	0.80	≤2.15	25.4	6.1	3.0 to 12.2

Adapted from Neves et al., 2018. J. Dairy Sci 101: 9321-9331.

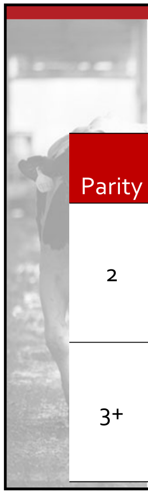
Milk results – primiparous cows

- Reduced tCa at 1 DIM associated with increased milk

DIM	n	*P*-value	AUC	Cut point, mmol/L	% below cut point	Milk yield, lb/d
1	137	0.01	0.57	≤2.15	40.0	6.4 (±1.8)

Adapted from Neves et al., 2018. J. Dairy Sci 101: 9321-9331.

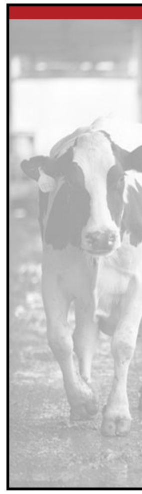
- No association of tCa at 2, 3, or 4 DIM with milk yield



Disease results – multiparous cows

- Association with metritis and/or DA differed by parity

Parity	DIM	n	*P*-value	AUC	Cut point, mmol/L	% below cut point	RR	95% CI
2	1	105	0.17	—	—	—	—	—
	2	105	<0.001	0.67	≤1.97	20.0	4.1	1.8 to 9.5
	3	104	0.24	—	—	—	—	—
	4	103	0.25	—	—	—	—	—
3+	1	151	0.17	—	—	—	—	—
	2	151	0.50	—	—	—	—	—
	3	151	0.60	—	—	—	—	—
	4	148	0.04	0.70	≤2.20	43.2	3.1	1.4 to 6.8



Milk results – multiparous cows

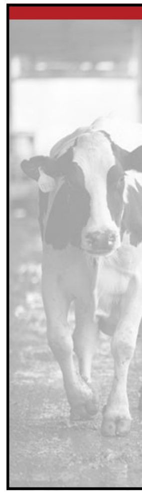
- Association of tCa with milk yield differed by DIM
  - Reduced tCa at 1 DIM associated with <u>increased</u> milk yield
  - Reduced tCa at 4 DIM associated with <u>decreased</u> milk yield

DIM	n	*P*-value	AUC	Cut point, mmol/L	% below cut point	Milk yield, lb/d
1	256	0.002	0.61	≤1.77	23.5	5.7 (±1.8)
4	251	0.04	0.52	≤2.20	39.0	-4.0 (±1.8)

Adapted from Neves et al., 2018. J. Dairy Sci 101: 9321-9331.

Conclusions

- <u>Day in milk</u> at time of testing and <u>parity</u> are important factors when characterizing SCH!
  - Parity 1 cows at 2 DIM
  - Parity 2 cows at 2 or 4 DIM → ???
  - Parity 3+ cows at 4 DIM
- Need more large field studies to validate these thresholds



Implications for the real world …

- We need to stop diagnosing SCH at 1 DIM.
- Should we evaluate herd-level calcium status based on parity group?
- What is a practical testing strategy in commercial herds?

Measure total calcium at 2-4 DIM

- Does postpartum calcium supplementation affect longer-term calcium homeostasis?

Determining Calcium Status

Cold ears?

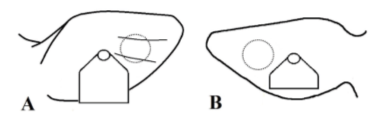
J. Dairy Sci. 99:6542–6549
http://dx.doi.org/10.3168/jds.2015-10734

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

P. L. Venjakob,*† S. Borchardt,* G. Thiele,† and W. Heuwieser*[1]
*Clinic for Animal Reproduction, Faculty of Veterinary Medicine, Freie Universität Berlin, Koenigsweg 65, 14163 Berlin, Germany
†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	39.0	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

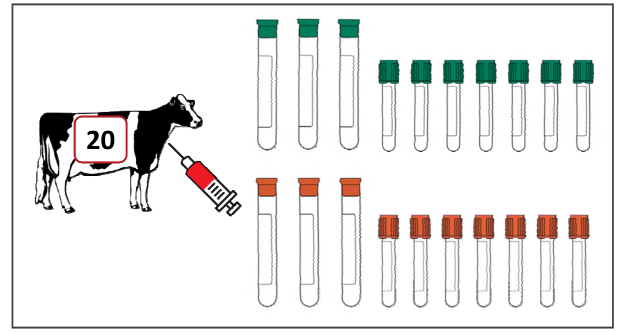
Direct measurement of calcium

- 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

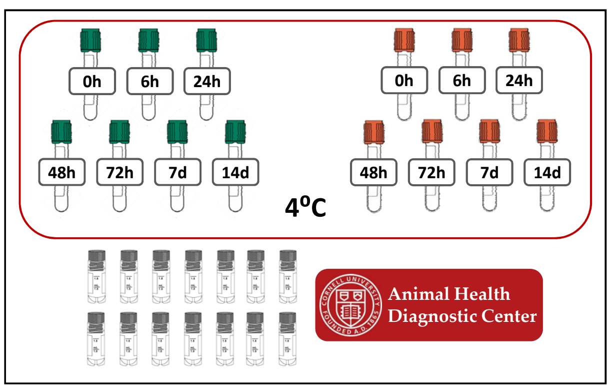
- Collect in green or red top tubes
- Fairly stable
- Methods of analysis:
  - Benchtop analyzer in laboratory @ $5-15/sample
  - Analyzer in vet clinic @ $5-7.50/sample

Study design



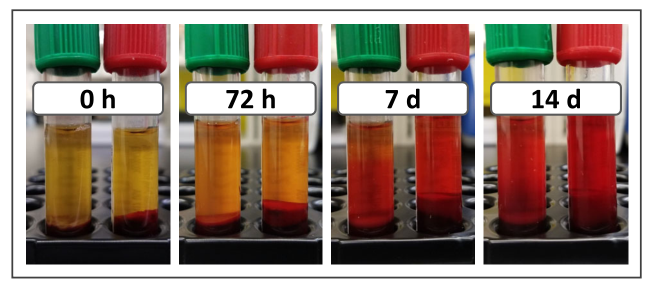
Courtesy: Kathryn Bach

Study design



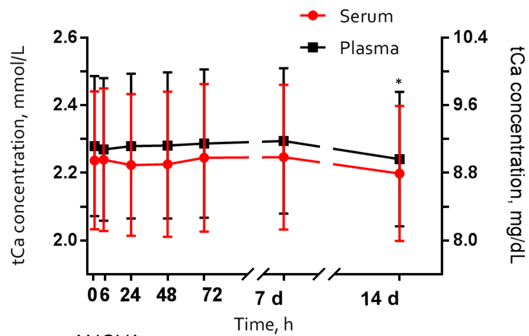
Courtesy: Kathryn Bach

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

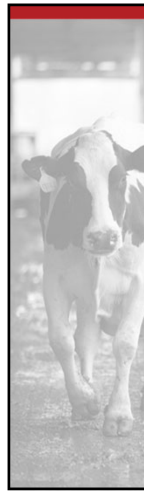
Ionized calcium – methods of analysis

- 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 do not currently exist
- Why not just measure tCa?
  - Relationship between tCa and iCa varies following parturition (Leno et al., 2017, J. Dairy Sci)

Postpartum calcium supplementation

Treatment/prevention options:

- Calcium borogluconate 23% (~10 g Ca)
  - Intravenous
  - Subcutaneous
- Oral drench with calcium propionate
  - 1 lb
  - Not practical
- Oral boluses
  - 40 – 50 g calcium
  - Different release speeds
- Oral gels



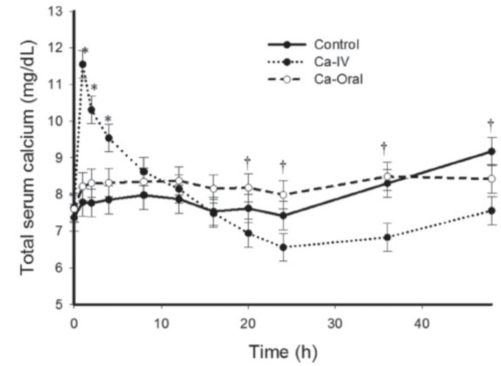
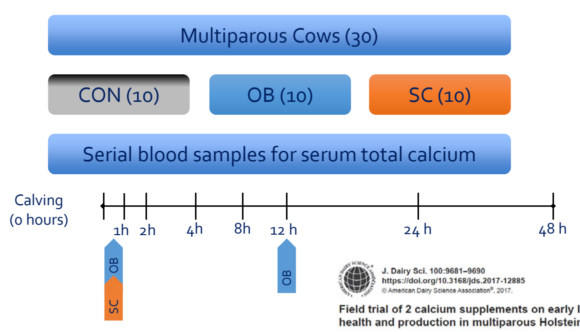


Figure 1. Total serum Ca levels (LSM ± SEM) after postpartum prophylactic treatment of subclinical hypocalcemia in control (no Ca supplementation; n = 11), intravenous Ca [Ca-IV, 500 mL of 23% calcium gluconate (Durvet, Blue Springs, MO) at postpartum; n = 11], and oral Ca [Ca-Oral, 2 Bovikalc (Boehringer Ingelheim, St. Joseph, MO) boluses 12 h apart at postpartum; n = 11)]. We detected a significant ($P < 0.001$) effect of time and treatment × time interaction. Significant treatment × time differences at each time point are indicated by † ($P < 0.05$) and * ($P < 0.001$).

Journal of Dairy Science Vol. 97 No. 11, 2014

Blanc et al., *JDS*, 2014

Aim: To observe serum Ca concentrations during the first 48 h postpartum in cows supplemented with oral Ca or subcutaneous Ca and non-supplemented cows



J. Dairy Sci. 100:9681–9690
https://doi.org/10.3168/jds.2017-12885
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Field trial of 2 calcium supplements on early lactation health and production in multiparous Holstein cows

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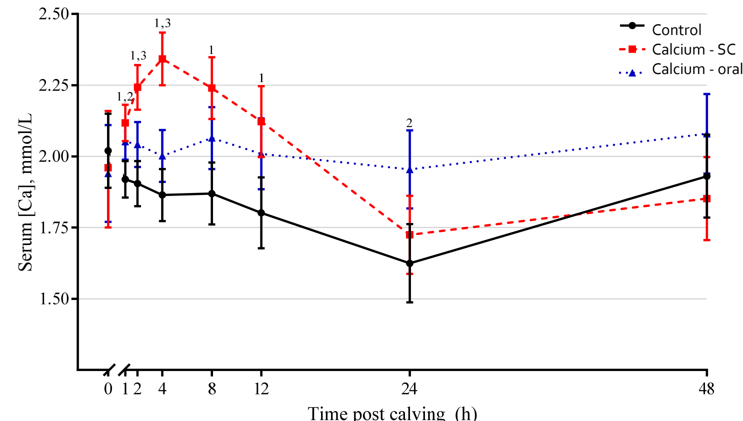
Department of Population Medicine and Diagnostic Sciences, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853

Courtesy of A. R. Domino



Domino et al., *JDS*, 2017

So, what is best?

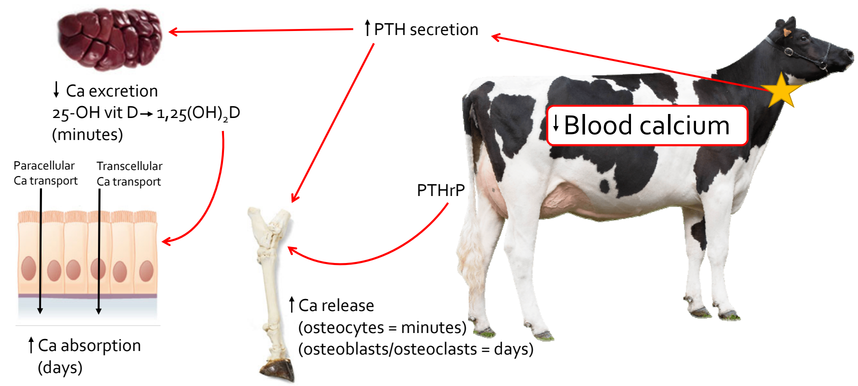
- Subcutaneous calcium? Oral calcium? Nothing?
  - Increase blood calcium for a short period of time
  - Does supplementation prevent disease or improve milk yield?
- Answer: it depends.
  - Blanket therapy not always beneficial
  - Target groups: high producing cows, older cows, lame cows, cows with difficulty calving
  - Avoid other groups: primiparous cows

Prevention

Nutritional strategies to reduce hypocalcemia

- Prepartum nutrition:
  - Feeding a dietary cation anion difference diet
  - Feeding a low Ca diet
    - Ca < 20g/d absorbed (practically difficult)
    - Calcium binder
- Postpartum nutrition:
  - Ensure adequate minerals

Increasing blood calcium



Altering blood pH via DCAD

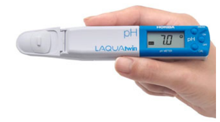
↓ Cations: Sodium (+1), Potassium (+1) + ↑ Anions: Chloride (-1), Sulfur (-2) = More H^+ in blood to maintain electroneutrality = decreased pH

- Improved sensitivity of PTH receptor to PTH stimulation
- Increased urinary Ca excretion = increased Ca flux
- May result in greater bone resorption and/or increased intestinal Ca absorption

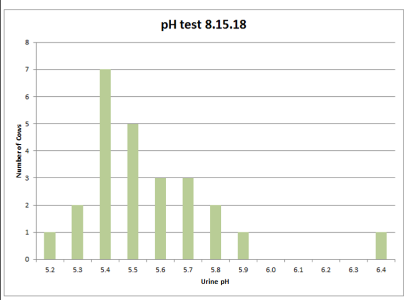
Courtesy of Brittany Leno

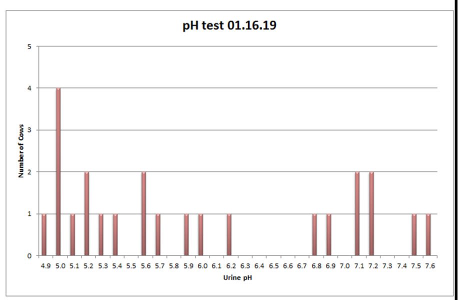
Goff et al., 2014; Goff and Horst, 2003; Martin-Tereso and Verstegen, 2011

Is the DCAD working?



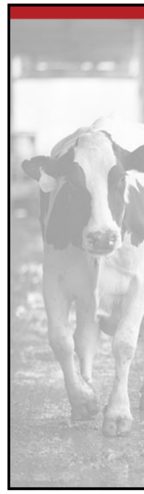
- Urine pH:
  - Midstream urine samples
  - Measure ~12 to 15 cows weekly
  - Consistent measurement relative to feeding time
- Goals:
  - 80% cows between 5.5 – 6.5
  - CV < 8%





- Median urine pH = 5.5 (5.2-6.4)
- 60% of cows between 5.5 – 6.5
- CV = 4.4%

- Median urine pH = 5.7 (4.9-7.6)
- 25% of cows between 5.5 – 6.5
- CV = 15.8%

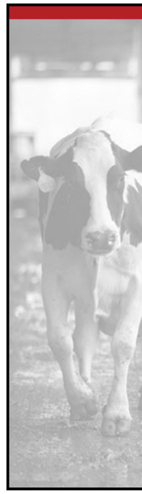


Feeding DCAD

- Feeding DCAD but normal urine pH values?
  - Cows not consuming expected DM or TMR not mixed properly
  - Improper evaluation and adjustment for other free-choice minerals or forage content
- Large variation between cows may indicate unequal consumption of ration.
  - Overcrowding or social factors
  - Sorting due to poor mixing

Feeding DCAD

- Variation between <u>weeks</u> can indicate inconsistency in ration mixing or changes in feed ingredient composition.
- Use this information to improve feeding and management strategies!



Calcium binders

- Sodium aluminum silicate (Zeolite A)
  - Can bind dietary Ca, P, Mg
  - Show to increase active form of vitamin D prepartum
  - Studies done in USA and New Zealand
    - Targeted 500 g/d as fed
- Decreased prevalence of hypocalcemia
- No change in postpartum milk yield

Summary ...

- Hypocalcemia is a normal occurrence in immediate postpartum dairy cows.
- Diagnostic testing is expensive – use your money wisely.
- Calcium supplementation is beneficial to an important group cows – the key is determining which group needs it and when!
- Prevention is always better than treatment.

<u>Goal</u>: identify optimal strategies to monitor and prevent hypocalcemia

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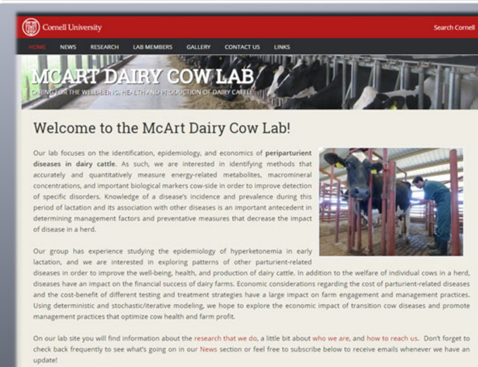
Questions?



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