Re-evaluating Transition Cow Dogmas, is the Nutritionist Really to Blame for the Problems

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Nutrition is Often Incorrectly Blamed for:

- High NEFA
- Hyperketonemia
  - Clinical and subclinical ketosis
- Subclinical hypocalcemia

- These are due to 1 of 2 things:
  - High productivity in healthy cows (profitable dairy producer)
    - The nutritionist deserves a raise
  - Metabolic reflection of immune activation
    - Likely stemming from metritis, mastitis, pneumonia or GIT inflammation
      - These are mostly management issues and not caused by nutrition

Everything in today's talk is thoroughly covered in our recent review

Horst et al., 2021, JDS 14:8380-8410

J. Dairy Sci. 104:8380–8410
https://doi.org/10.3168/jds.2021-20330

Invited review: The influence of immune activation on transition cow health and performance—A critical evaluation of traditional dogmas

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ABSTRACT

The progression from gestation into lactation represents the transition period, and it is accompanied by marked physiological, metabolic, and inflammatory adjustments. The entire lactation and a cow's opportunity to have an additional lactation are heavily dependent on how successfully she adapts during the periparturient period. Additionally, a disproportionate amount of health care and culling occurs early following parturition. Thus, lactation maladaptation has been a heavily researched area of dairy science for more than 50 yr. It

feed intake and causes hypocalcemia. Our tenet is that immune system utilization of glucose and its induction of hypophagia are responsible for the extensive increase in NEFA and ketones, and this explains why they (and the severity of hypocalcemia) are correlated with poor health, production, and reproduction outcomes. In this review, we argue that changes in circulating NEFA, ketones, and calcium are simply reflective of either (1) normal homeorhetic adjustments that healthy, high-producing cows use to prioritize milk synthesis or (2) the consequence of immune activation and its sequelae.
Key words: inflammation, hypocalcemia, ketosis,

Guiding Concepts and Principles

- The best indicators of “health” are feed intake and milk yield.
- Everyone agrees that “stress” reduces productivity……..
  then high productivity CANNOT be stressful
- We have over complicated animal health
  - Cows that are eating and producing large quantities of milk ARE healthy
- The progressive dairy industry is ahead of academia
  - With regards to transition cow management
    - Large successful dairy farms are already doing everything I’m talking about
- Inconsistent and unreproducible data should create doubt
  - When scientific papers do not agree we should be skeptical

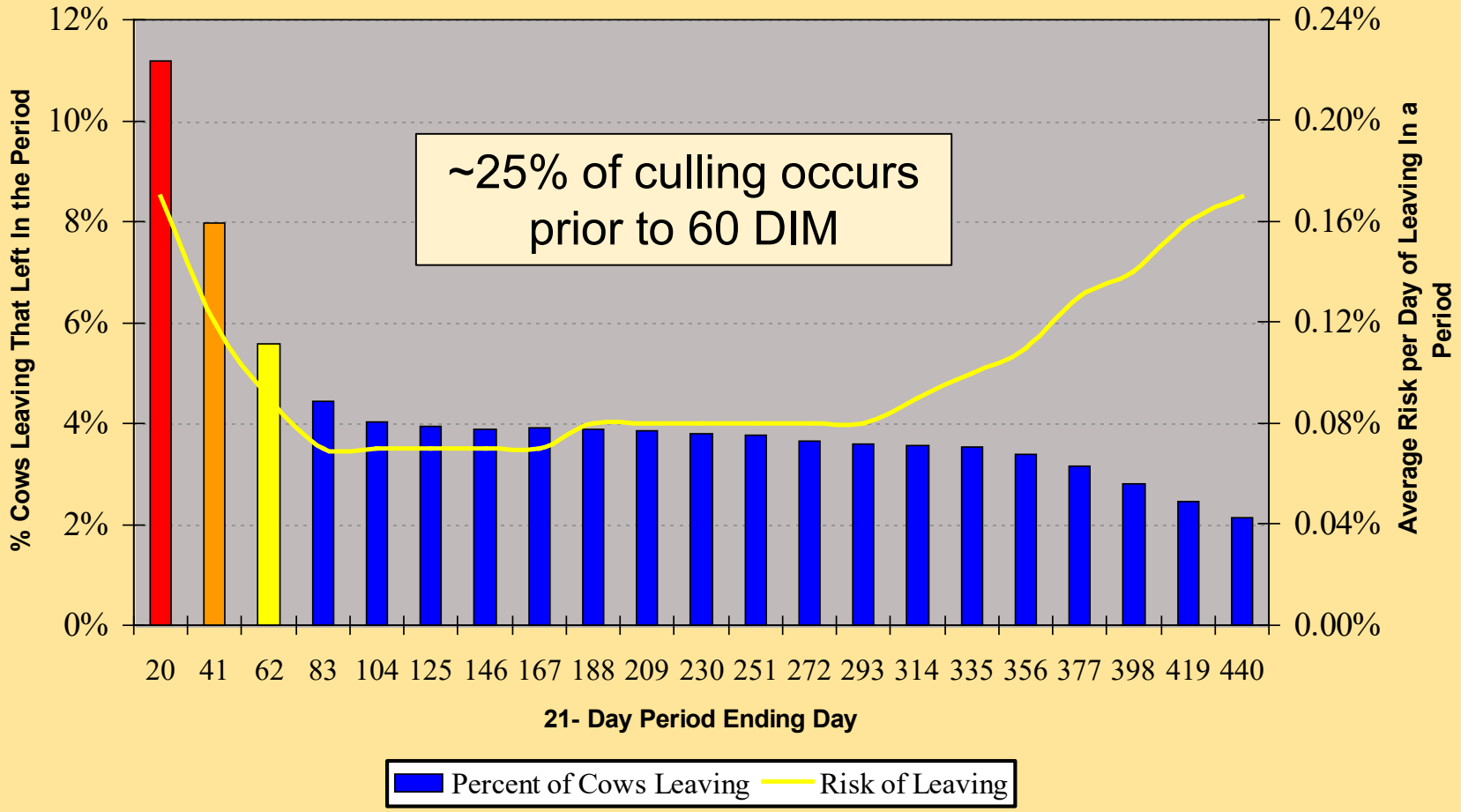
Transition Period Morbidity

Disorders affects 50%:

- Dystocia
- Milk fever
- Retained placenta
- Metritis
- Ketosis
- DA
- Fatty liver
- Lameness
- Death

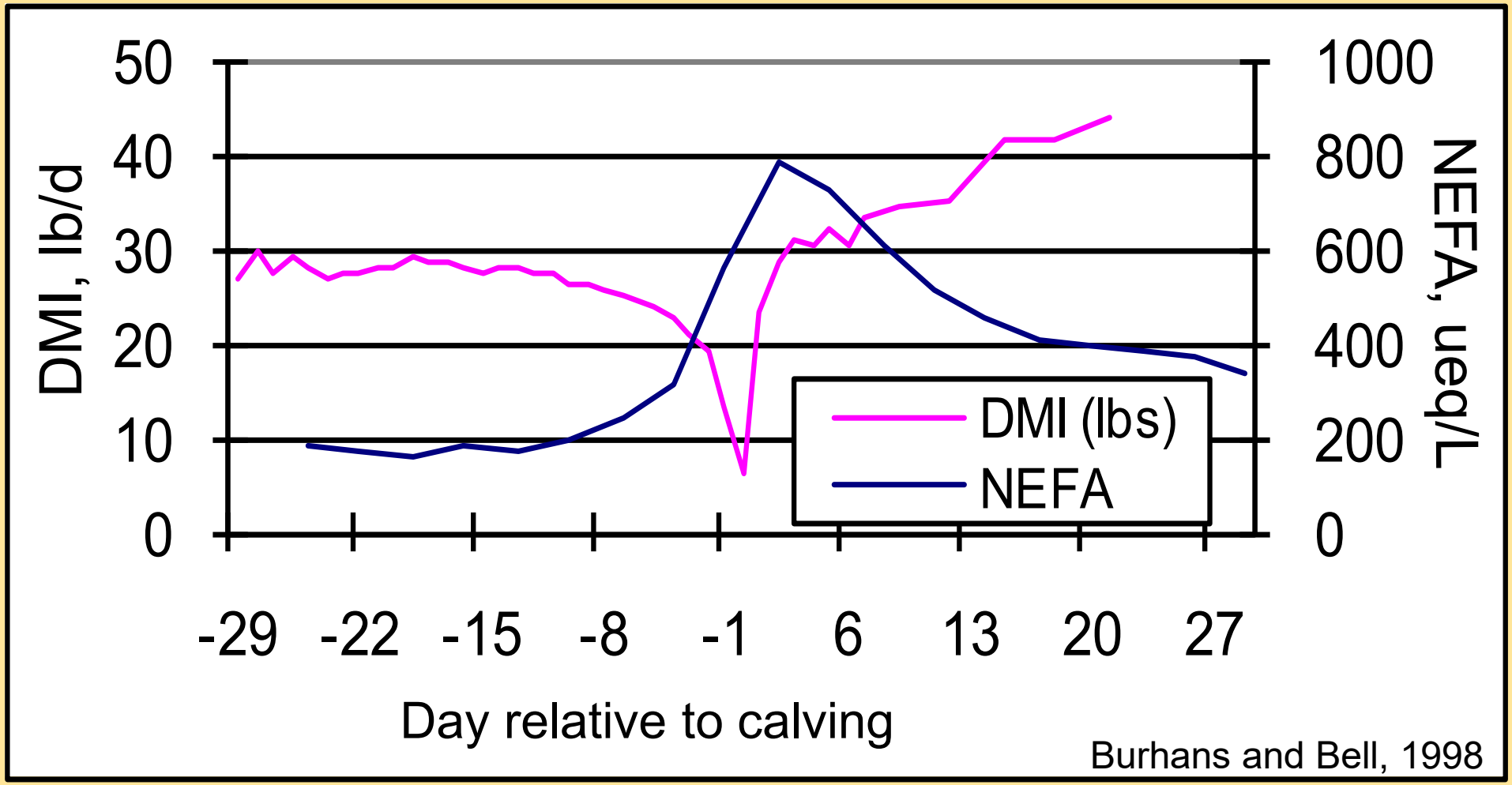
Drackley, 1999

When cows leave the herd

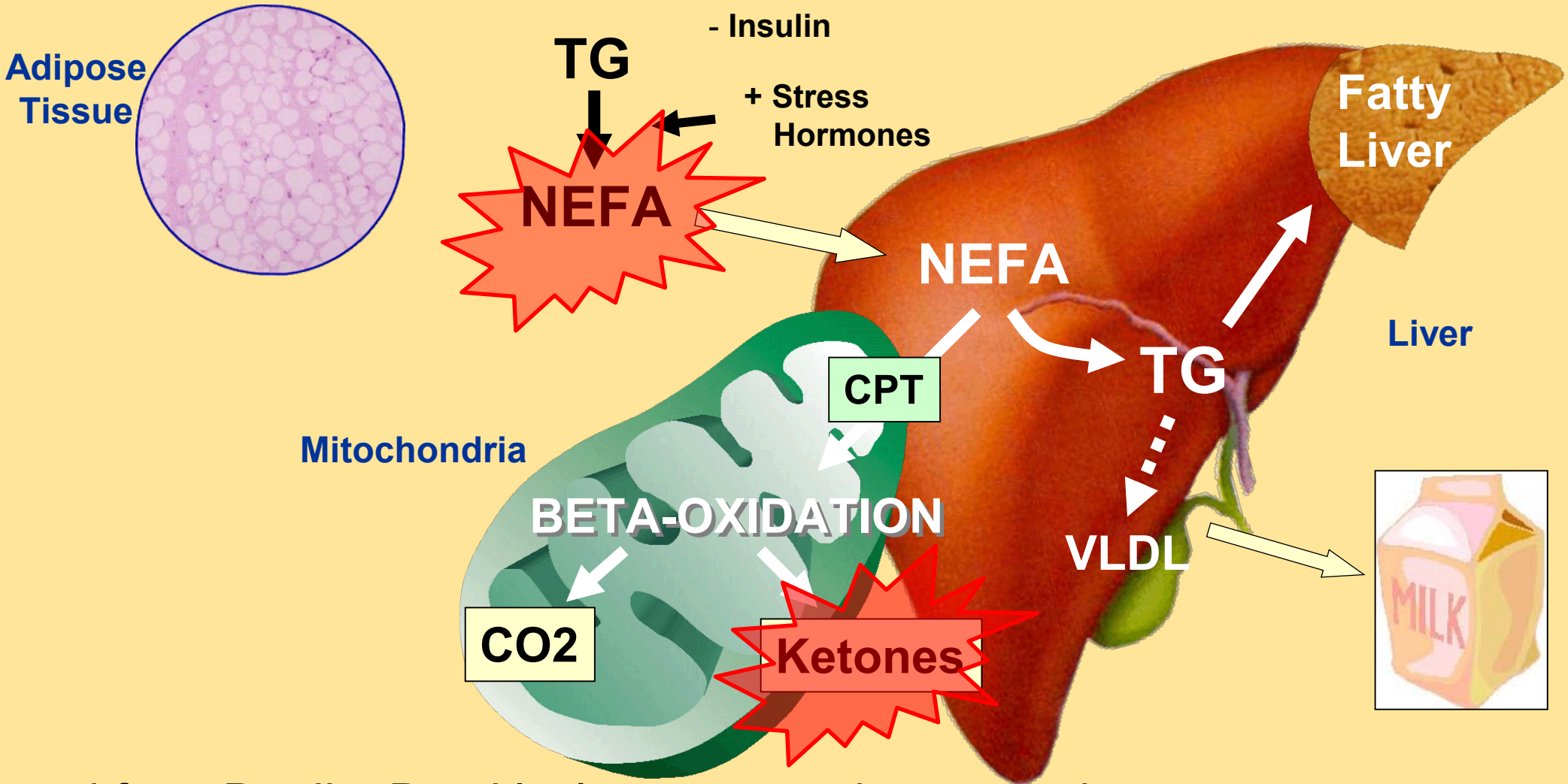


Source: 2002, Steve Stewart, DVM, Dipl.-ABVP, Univ. of Minnesota, College of Vet. Med.

Transition Period Energy Balance



Liver Lipid Metabolism During the Transition Period



Adapted from Dr. Jim Drackley's papers and presentations

Retrospective and Observational Studies

- Hundreds of studies *associate* and correlate NEFA, BHBA and Ca with:
  - Increased risk of ketosis, decreased milk yield, LDA, metritis, retained placenta, laminitis, or poor reproduction
    - Chapinal et al., 2011; Huzzey et al., 2011; Ospina et al., 2010a, 2010c; Duffield et al., 2009; LeBlanc et al., 2005
- Many papers do not agree…..inconsistencies in the literature
  - Unlike the overwhelming and converging lines of evidence demonstrating smoking causes cancer.
    - Claiming NEFA and ketone skepticism is akin to questioning whether smoking causes cancer is bewildering
- Plasma NEFA are markedly increased (>700 mEq/L) following calving in almost all cows
  - ~15-20% get clinical ketosis
  - What makes these cows more susceptible to ketosis?
    - Predisposition to developing fatty liver?
- Reductionist approach (one metabolite = one disease)

Cause and Effect??

- The incidence of health problems is highest in the first month of lactation
- The largest swings in energetic metabolites, hormones and minerals occurs in the first month of lactation
- Thus…a lot of moving parts and events occurring simultaneously
  - Consequently they will all be correlated
- Causality and correlation are incorrectly interchanged when an observational relationship between 2 events is claimed to be inevitable rather than coincidental.

This correlation interpretation then causes suspect decision making and unnecessary farm expenses

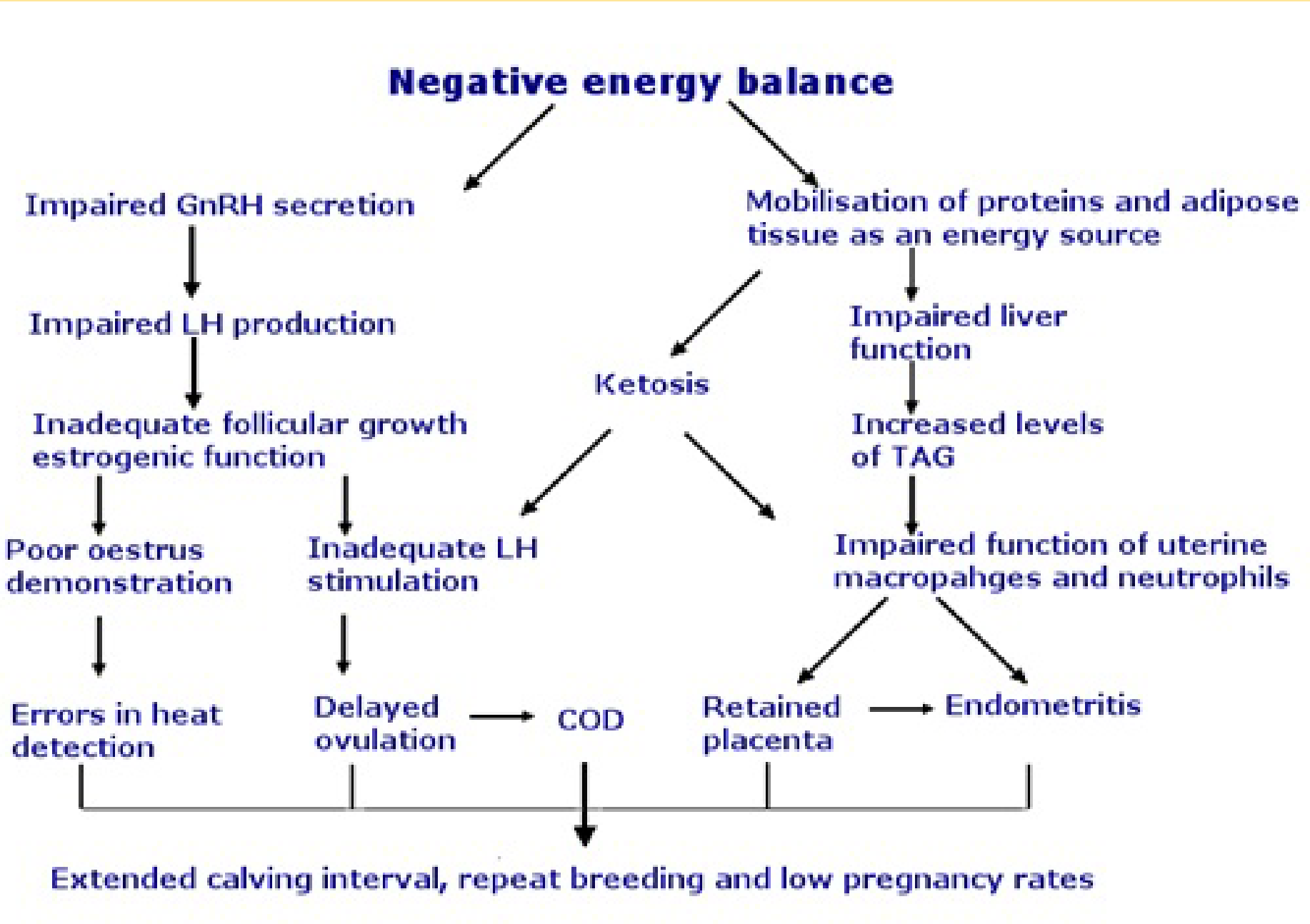
Traditional Belief

Assuming Correlation Equals Causation

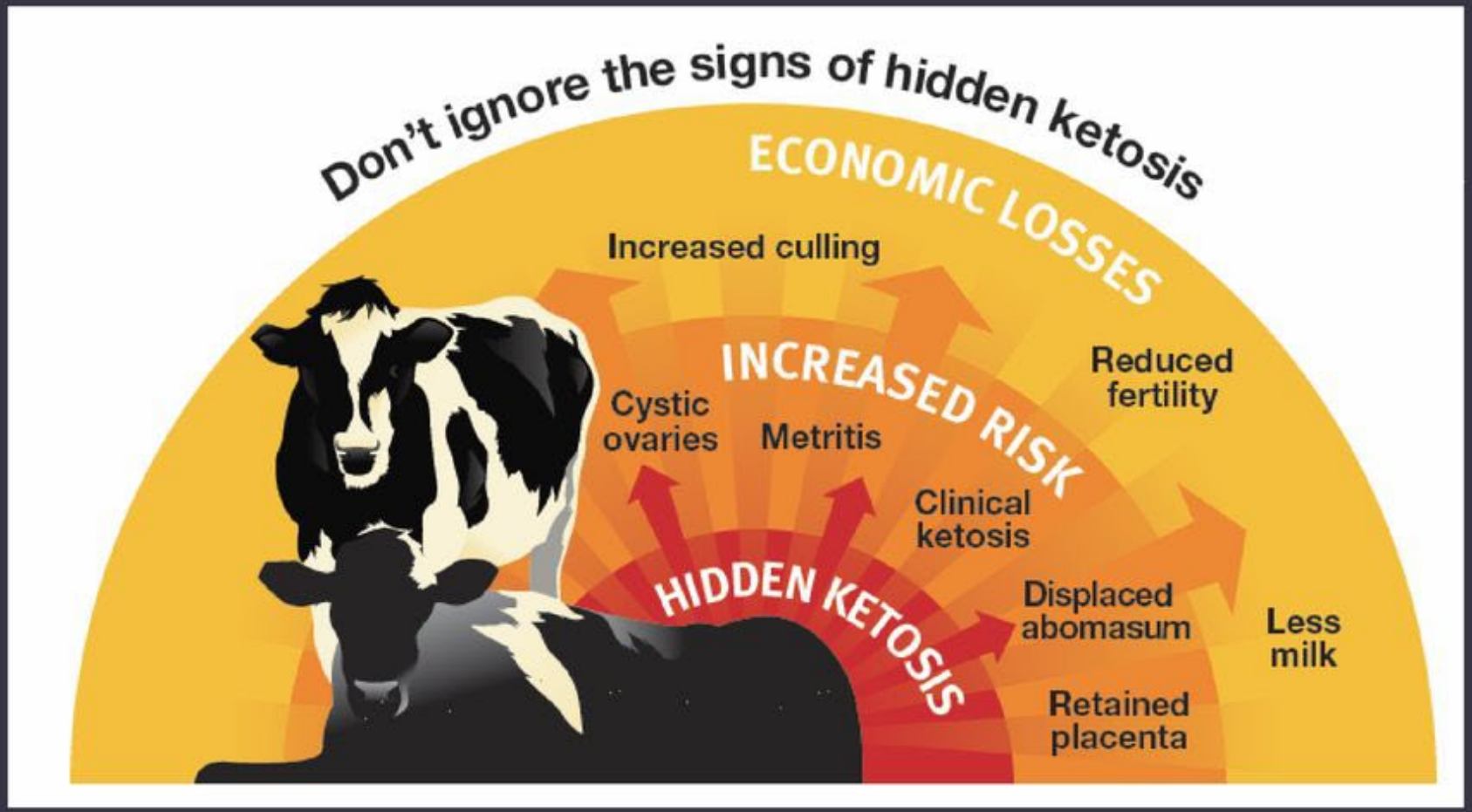
Increased NEFA, Hyperketonemia, and Hypocalcemia…..**CAUSE** production and health problems

Dogma: Negative Energy Balance CAUSES problems

An example model



Dogma: Ketones cause problems



https://slideplayer.com/slide/13774593/

How (and why) do NEFA, Hyperketonemia and Hypocalcemia cause problems

- Biological plausibility?
  - Why would evolution favor a scenario where the mother endangers herself and compromises her ability to nourish her young?

- There remains little mechanistic evidence for how NEFA, ketones and Ca can directly have such a large influence on a variety of seemingly unconnected systems and diseases

- Best line of evidence is extrapolated from their purported role in immunosuppression.

If hyperketonemia, high NEFA and subclinical hypocalcemia are pathological….it stands to reason that therapeutically treating these disorders would improve cow health

Culling Trends Over Time

Culling Reason	NAHMS (1996)	NAHMS (2002)	NAHMS (2014)
Voluntary Reasons	21.3	19.3	21.1
Re			
Injury	4.1	6.0	5.2
Death	3.8	4.8	4.2
Disposition			
Lameness	14.2	16.3	16.8
Other	3.9	4.1	

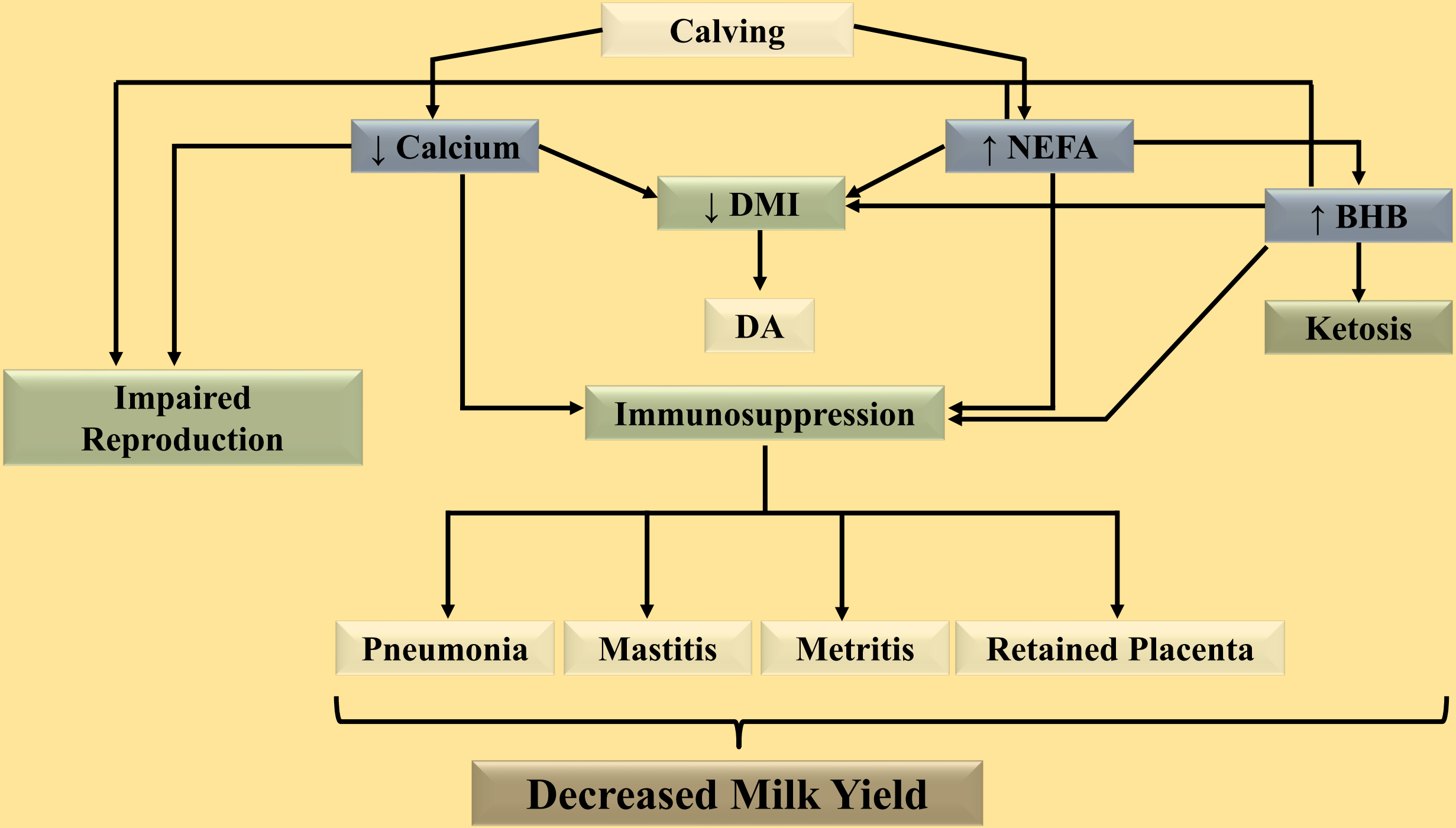
Despite emphasis, time and money spent on preventing high NEFA, hyperketonemia and subclinical hypocalcemia herd health is not improving

Maybe we're "medicating" the wrong things??

National Animal Health Monitoring Systems

Traditional Belief

Increased NEFA, Hyperketonemia, and Hypocalcemia…..**CAUSE** production and health problems


Calving
↓ Calcium
↑ NEFA
↓ DMI
↑ BHB
DA
Ketosis
Impaired Reproduction
Immunosuppression
Pneumonia
Mastitis
Metritis
Retained Placenta
Decreased Milk Yield

Partitioning of Nutrients During Pregnancy and Lactation: A Review of Mechanisms Involving Homeostasis and Homeorhesis

DALE E. BAUMAN and W. BRUCE CURRIE
Department of Animal Science
Cornell University
Ithaca NY 14853

Introduced the Homeorhesis concept

ABSTRACT

Control of metabolism during preg-
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tions and physiological processes in which food is transformed into body tissues and activities

Lave
a chem
sustenance involves a series of chemical reac-

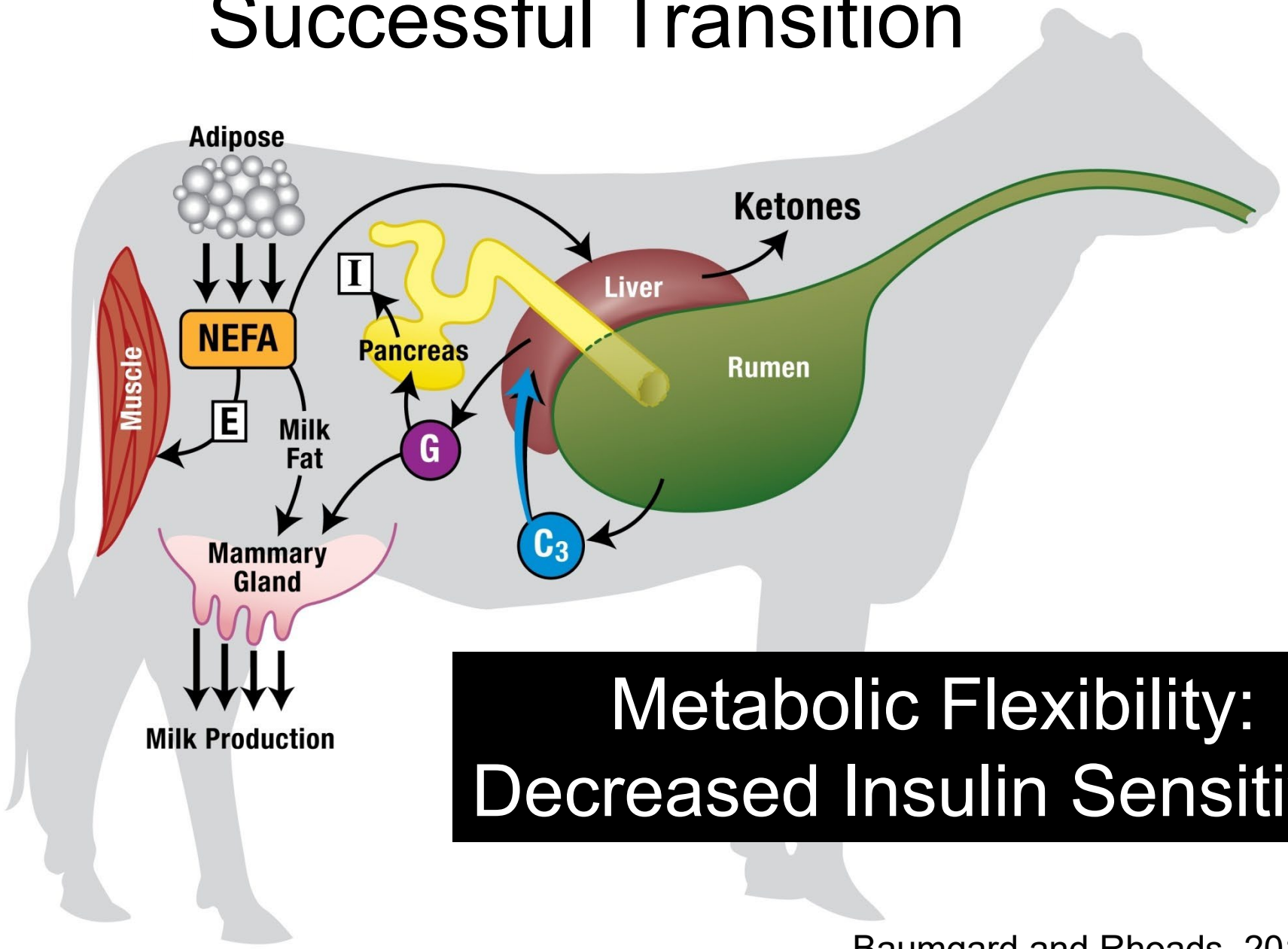
involves maintenance of physiological equilibri-
um or constant conditions in the internal environment (Figure 2). There are many well established examples of homeostasis, such as regulation to maintain constancy of body

Received January 28, 1980.

Summary of these Reviews

Mobilization of adipose tissue and partial conversion of NEFA into Ketones is ESSENTIAL for maximum milk yield in early lactation

Successful Transition



Metabolic Flexibility: Decreased Insulin Sensitivity

Baumgard and Rhoads, 2013

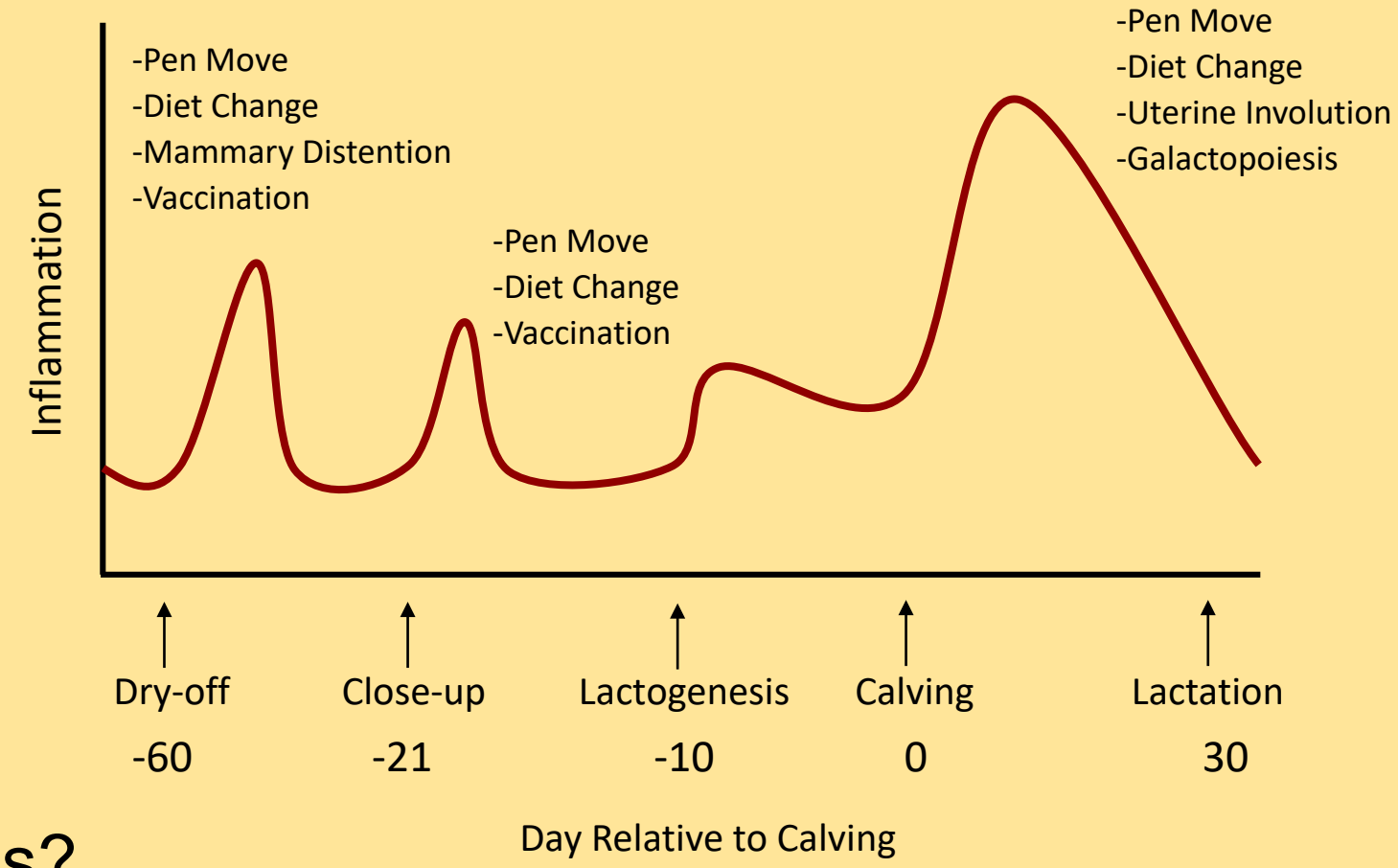
Inflammation in Transition Cows

- Observed in all cows

(Bertoni et al., 2008; Trevisi and Minuti, 2018)

- What is the source?
  - Mammary Gland
  - Uterus
  - Gastrointestinal tract

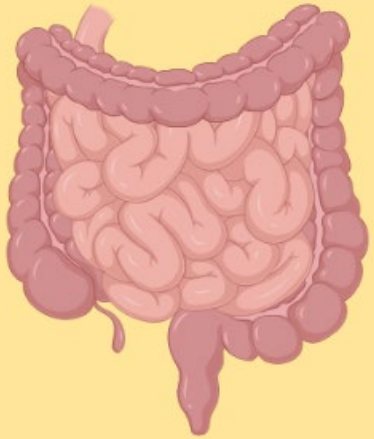
- What are the consequences?



Dr. B. Goetz

Inflammation sources:

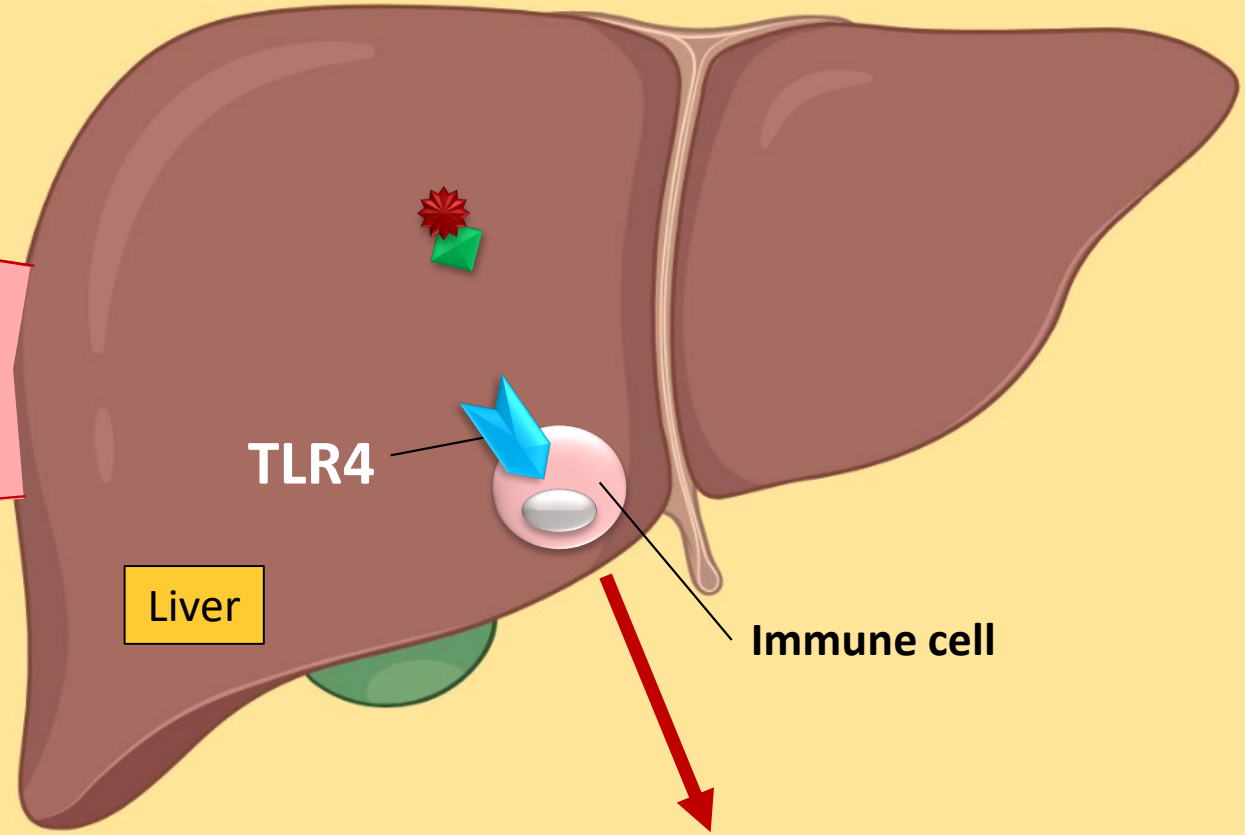
LPS



Complex LPS/LBP

LBP

Circulation

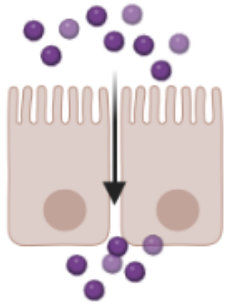


↑ Inflammatory response
↑ Cytokines
↑ APPs:
- SAA
- Hp
- LBP

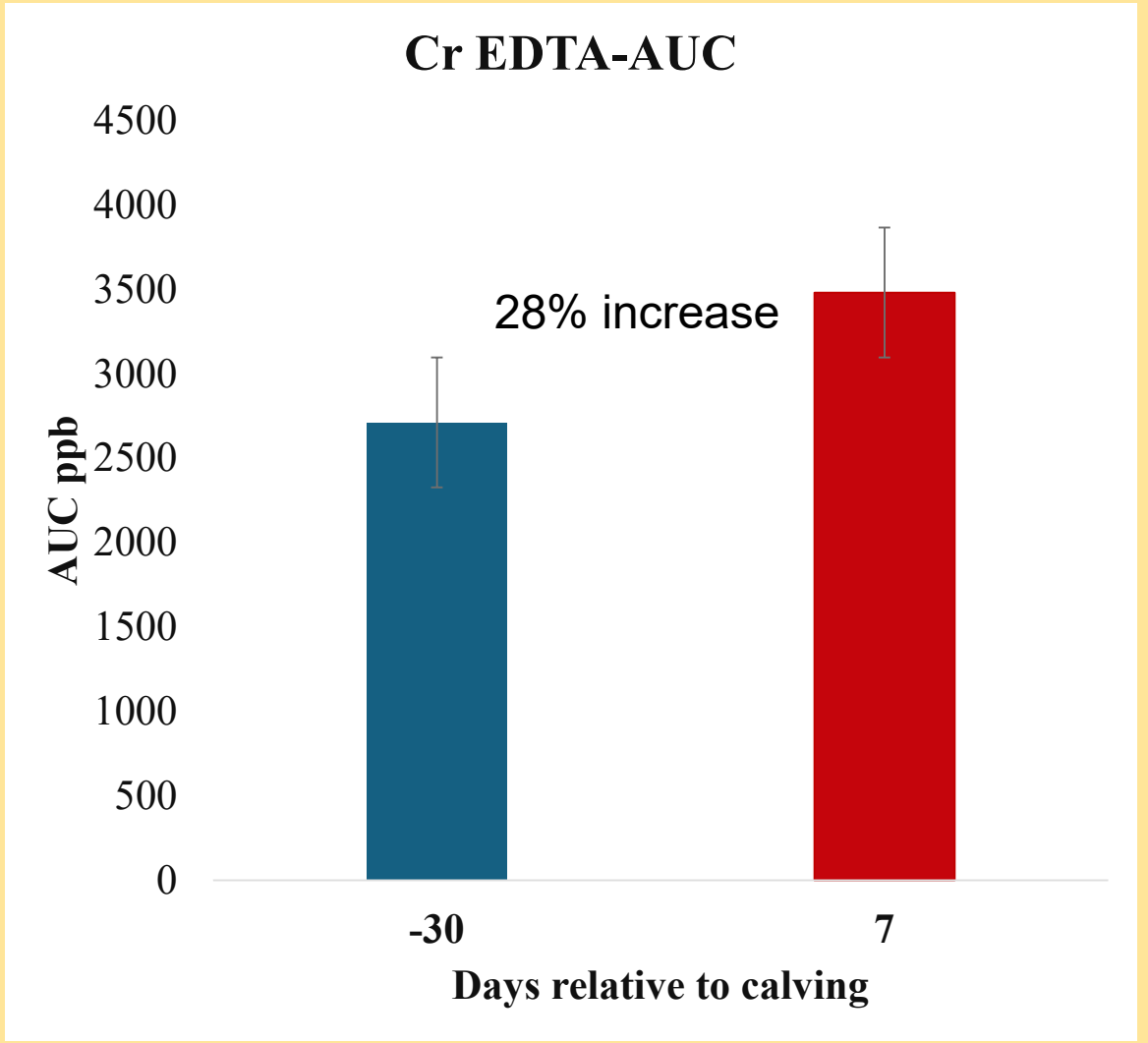
Rodriguez Jimenez & Kvidera

GIT Permeability Increases Post Calving

Professor Michael Steele

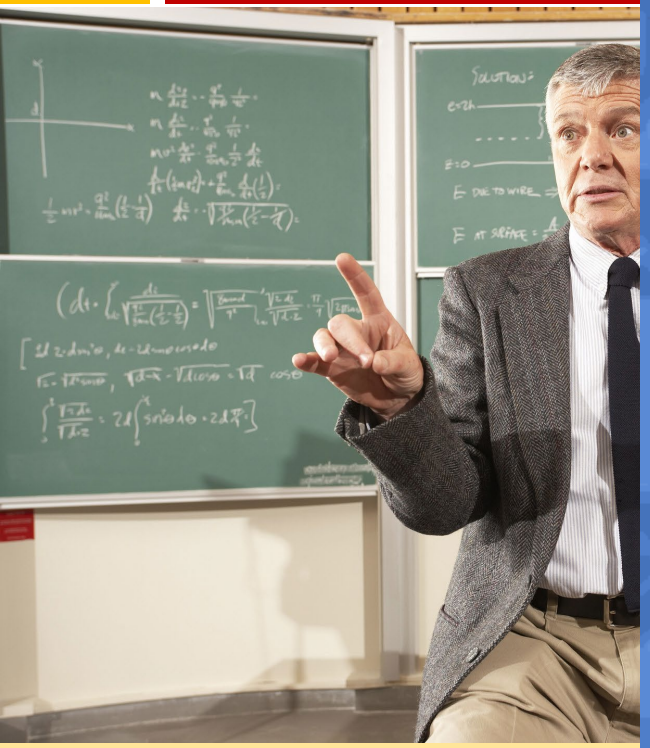


Gut permeability measurement based on Cr-EDTA recovery rate in plasma



Jantzi et al. (Unpublished data)

University vs. Commercial



Dr. Erin Horst

Elanco

TECHNICAL BRIEF

SCIENTIFIC UPDATE FROM ELANCO ANIMAL HEALTH

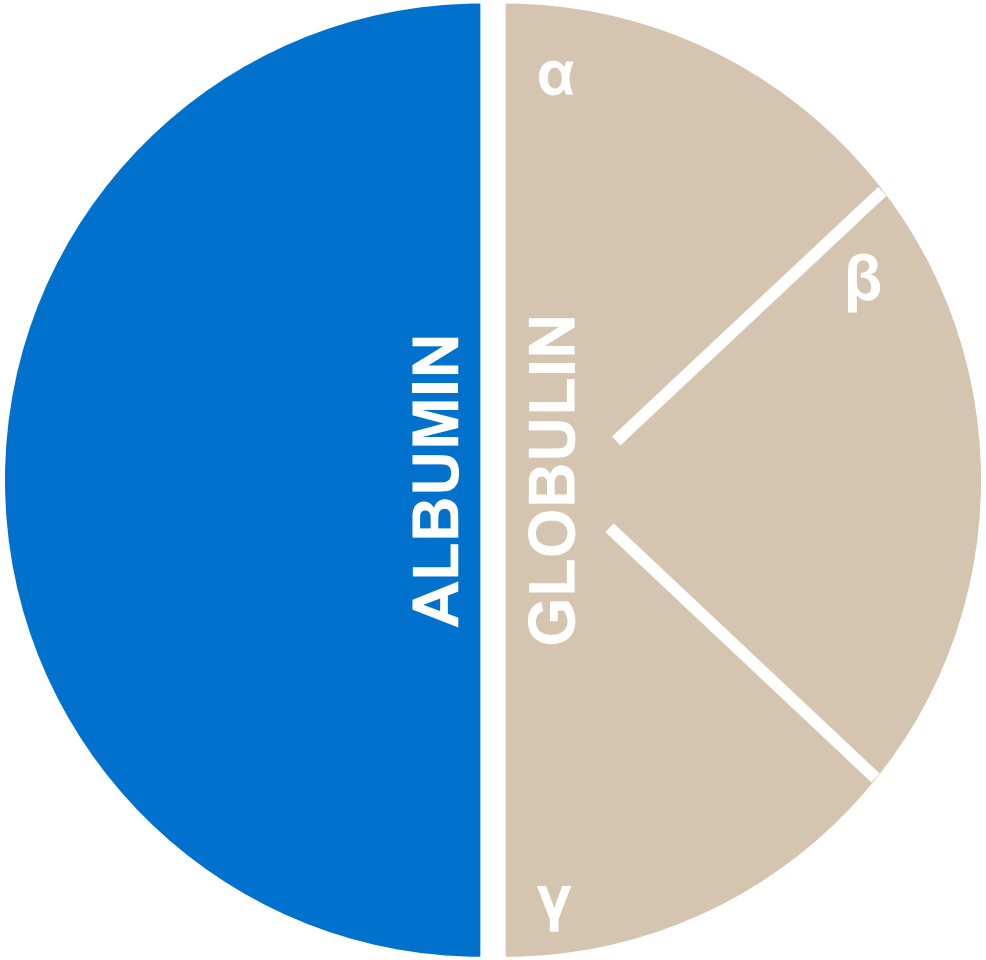
ASSOCIATION OF SERUM ALBUMIN TO GLOBULIN RATIO WITH HEALTH AND MILK PRODUCTION ON COMMERCIAL DAIRY HERDS

MATERIALS AND METHODS

A total of 370 cows from 19 herds (6 in Wisconsin, 6 in Michigan, 1 in Texas, and 6 in California) were enrolled in the study between June and August 2024. The selected herds were progressive, well-managed operations reporting no significant transition cow disease challenges. Blood samples were obtained from 6 to 36 cows per herd at 7±2 DIM for determination of the albumin-to-globulin ratio. At the time of blood collection, the selected cows exhibited no clinical signs of disease.

Albumin to Globulin Ratio (AGR)

- Most abundant constituent of plasma proteins (35-50%)
- Major carrier protein
- Classified as a negative acute phase protein (i.e., decreases during inflammation)



- Broad class of proteins made of 3 major fractions (α, β, γ)
- Includes the main positive acute phase proteins such as haptoglobin, ceruloplasmin, and serum amyloid A which increase during inflammation

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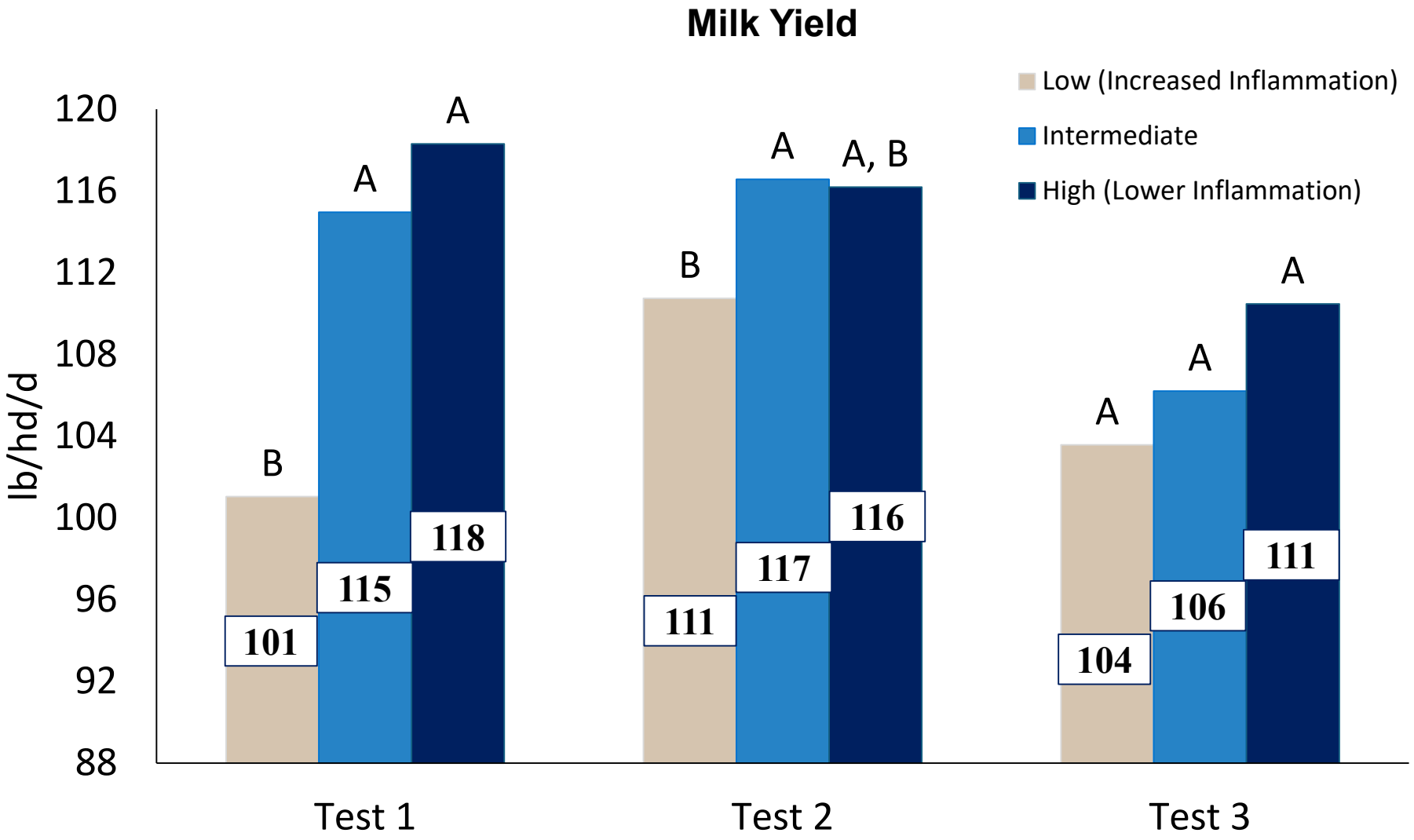
1st, 2nd, and 3rd, Milk Yield



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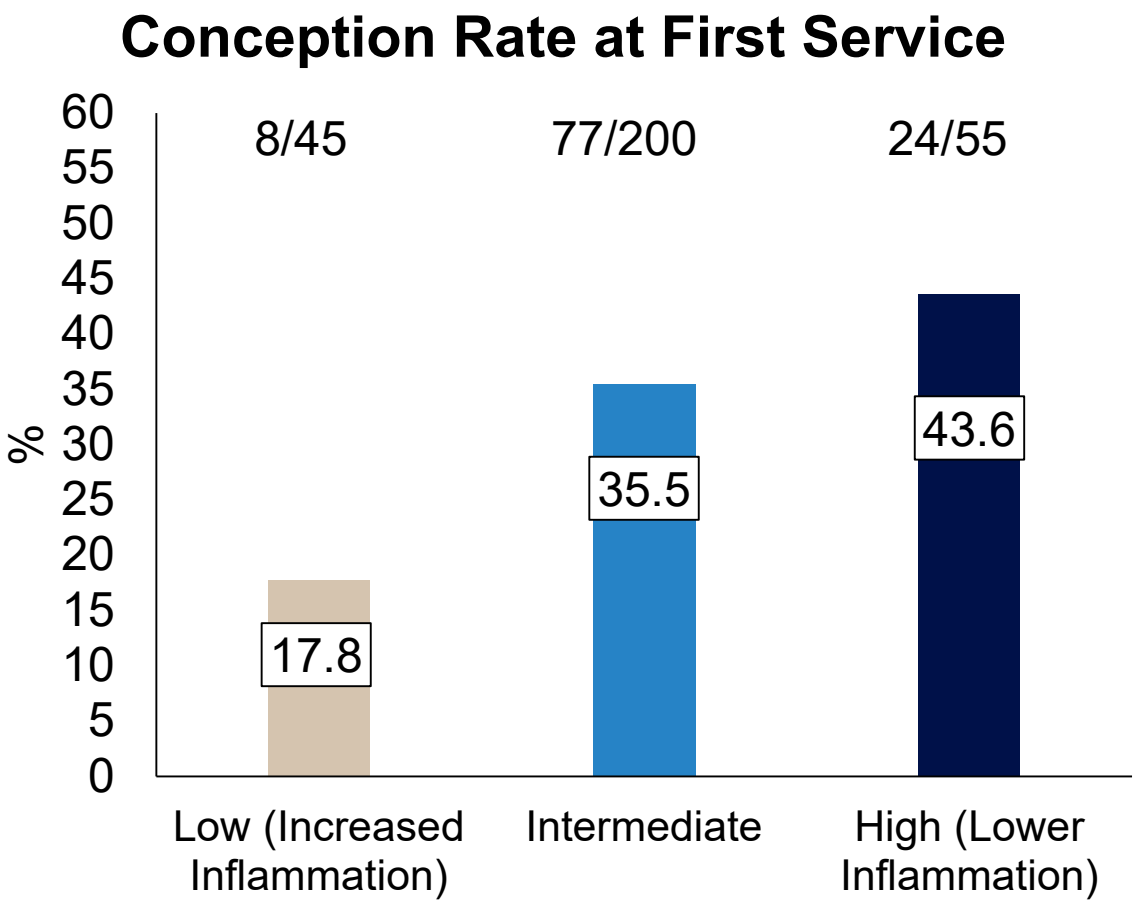
First Service Outcome



Odds Ratio			*P*-value	
H vs. I	H vs. L	I vs. L	AG	Dairy
1.075 (0.550-2.100)	2.007 (0.704-5.719)	1.866 (0.756-4.607)	0.35	<0.01

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TECHNICAL BRIEF

SCIENTIFIC UPDATE FROM ELANCO ANIMAL HEALTH

ASSOCIATION OF SERUM ALBUMIN TO GLOBULIN RATIO WITH HEALTH AND MILK PRODUCTION ON COMMERCIAL DAIRY HERDS

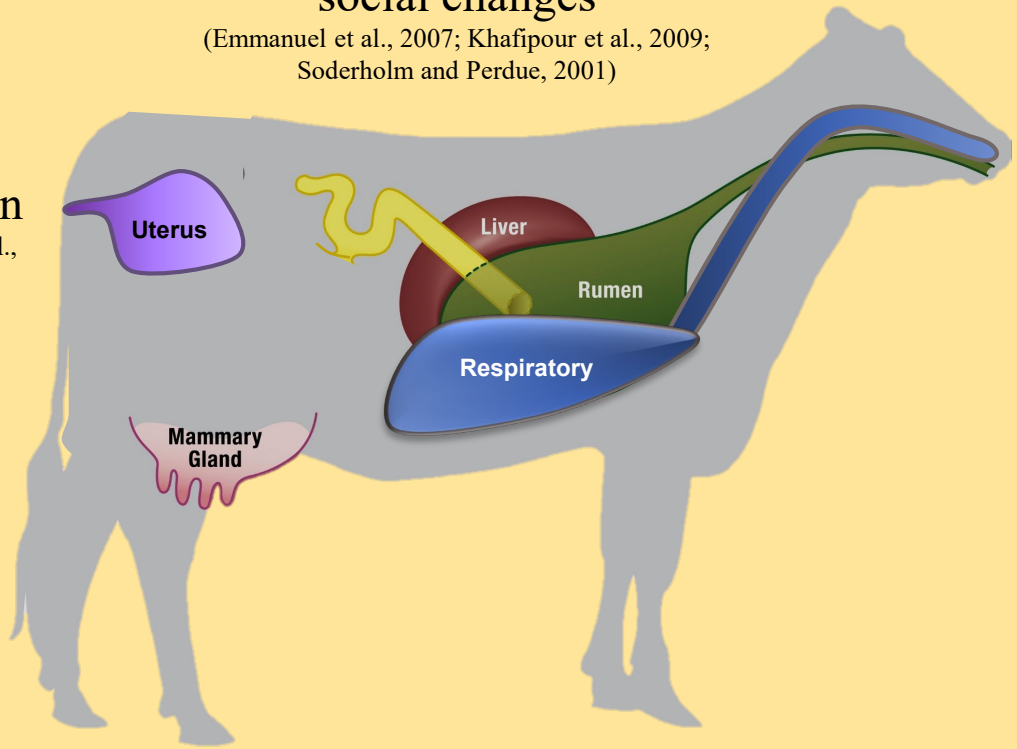
This suggests that gastrointestinal tract inflammation is a meaningful source of transition cow poor performance

A total of 370 cows from 19 herds (6 in Wisconsin, 6 in Michigan, 1 in Texas, and 6 in California) were enrolled in the study between June and August 2024. The selected herds were progressive, well-managed operations reporting no significant transition cow disease challenges. Blood samples were obtained from 6 to 36 cows per herd at 7±2 DIM for determination of the albumin-to-globulin ratio. At the time of blood collection, the selected cows exhibited no clinical signs of disease.

Heightened risk of antigen insult in early lactation

Increased gut permeability via diet and social changes
(Emmanuel et al., 2007; Khafipour et al., 2009; Soderholm and Perdue, 2001)

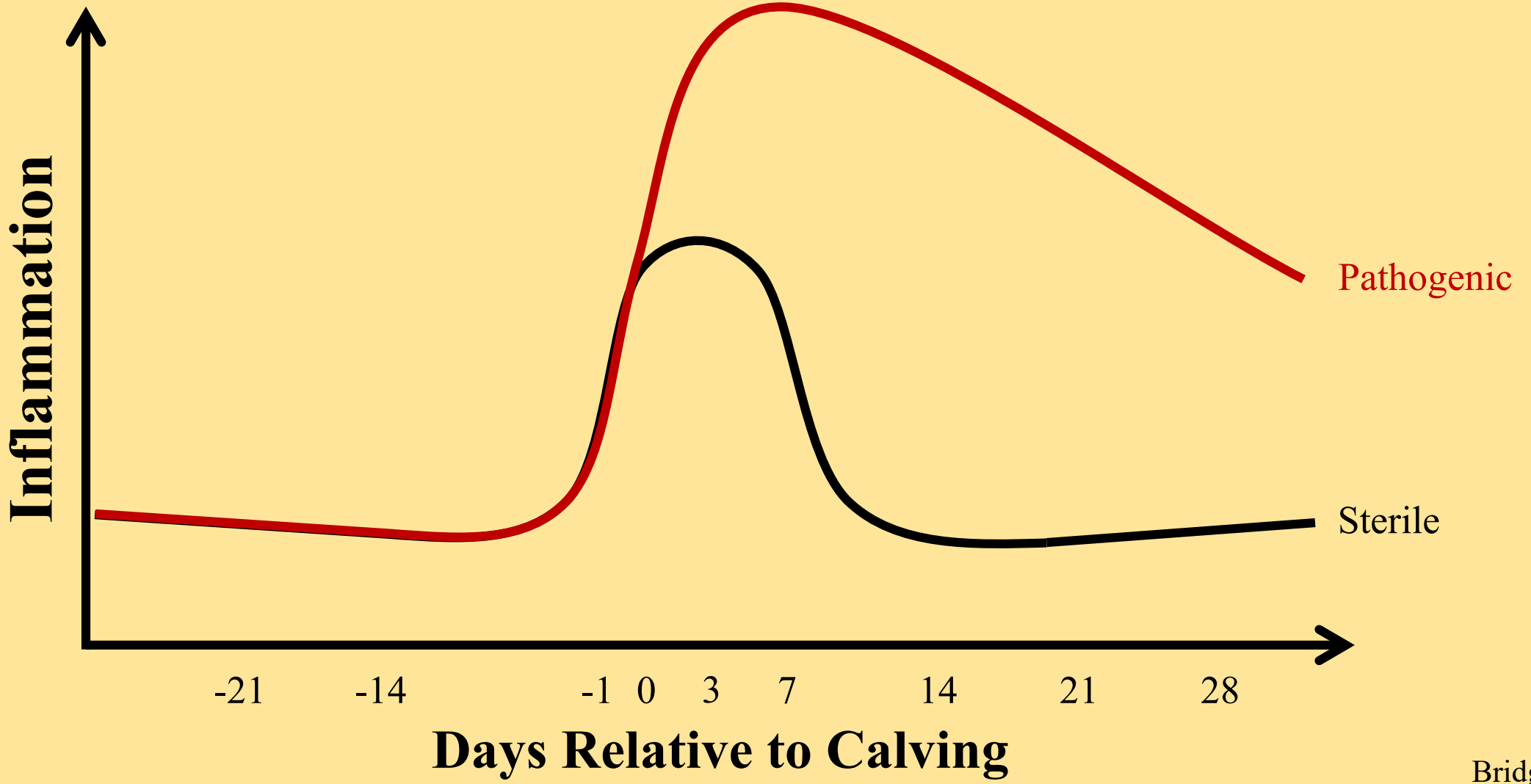
Uterine bacterial contamination post-parturition
(Paisley et al., 1986; Földi et al., 2006; Norman et al., 2007; Sheldon et al., 2008)



Lactogenesis and galactopoeisis
(Akers and Nickerson, 2011)

<u>Sterile Inflammation</u>
Parturition
Placenta Expulsion
Uterine Involution

Transition Cow Inflammation



Bridget Buol

Pathogenic Inflammation's Role in Suboptimal DMI

Immune activation induced hypophagia is KEY

Immune Activation and Feed Intake

- Inflammatory mediators are potent anorexic compounds Kushibiki et al., 2003
- Reduced feed intake is a highly conserved species response to infection (Aubert et al., 1997; Wang et al., 2016)
- Infection decreases feed consumption, even in insects (Adamo, 2005)
- Cows with increased inflammation have decreased DMI (Trevisi et al., 2002)
  - ….and also increased NEFA and BHB (Trevisi et al., 2010, 2012; Zhou et al., 2016)
  - **Inflammation is the simplest and most logical explanation for why some cows don't eat well before and following calving**

Inflammation and Fatty Liver??

World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/1007-9327office
wjg@wjgnet.com
doi:10.3748/wjg.v18.i21.2609

World J Gastroenterol 2012 June 7; 18(21): 2609-2618
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

REVIEW

Leaky gut and the liver: A role for bacterial translocation in nonalcoholic steatohepatitis

Yaron Ilan

- Humans with intestinal barrier dysfunction have fatty liver….but do not have increased [NEFA]

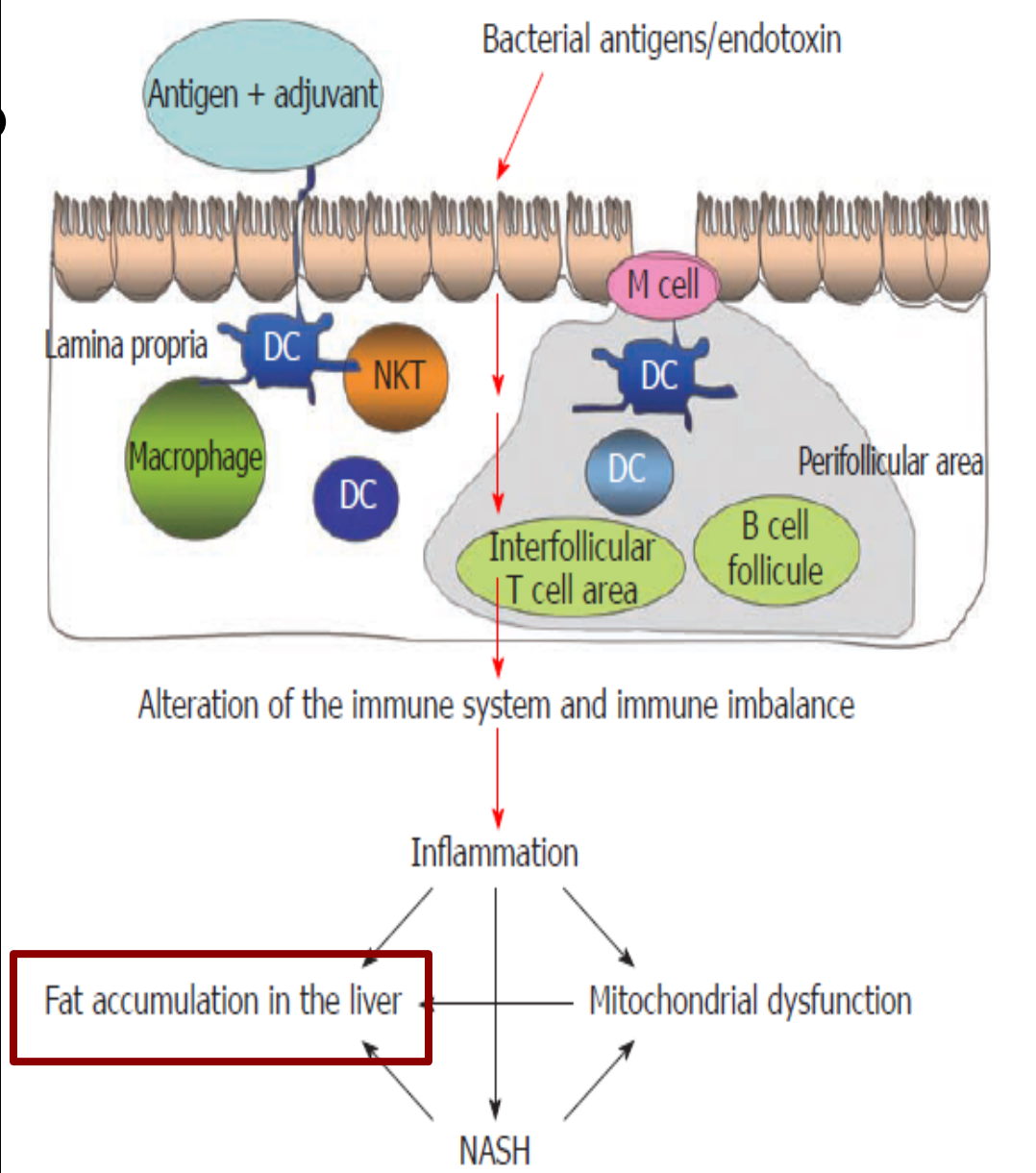
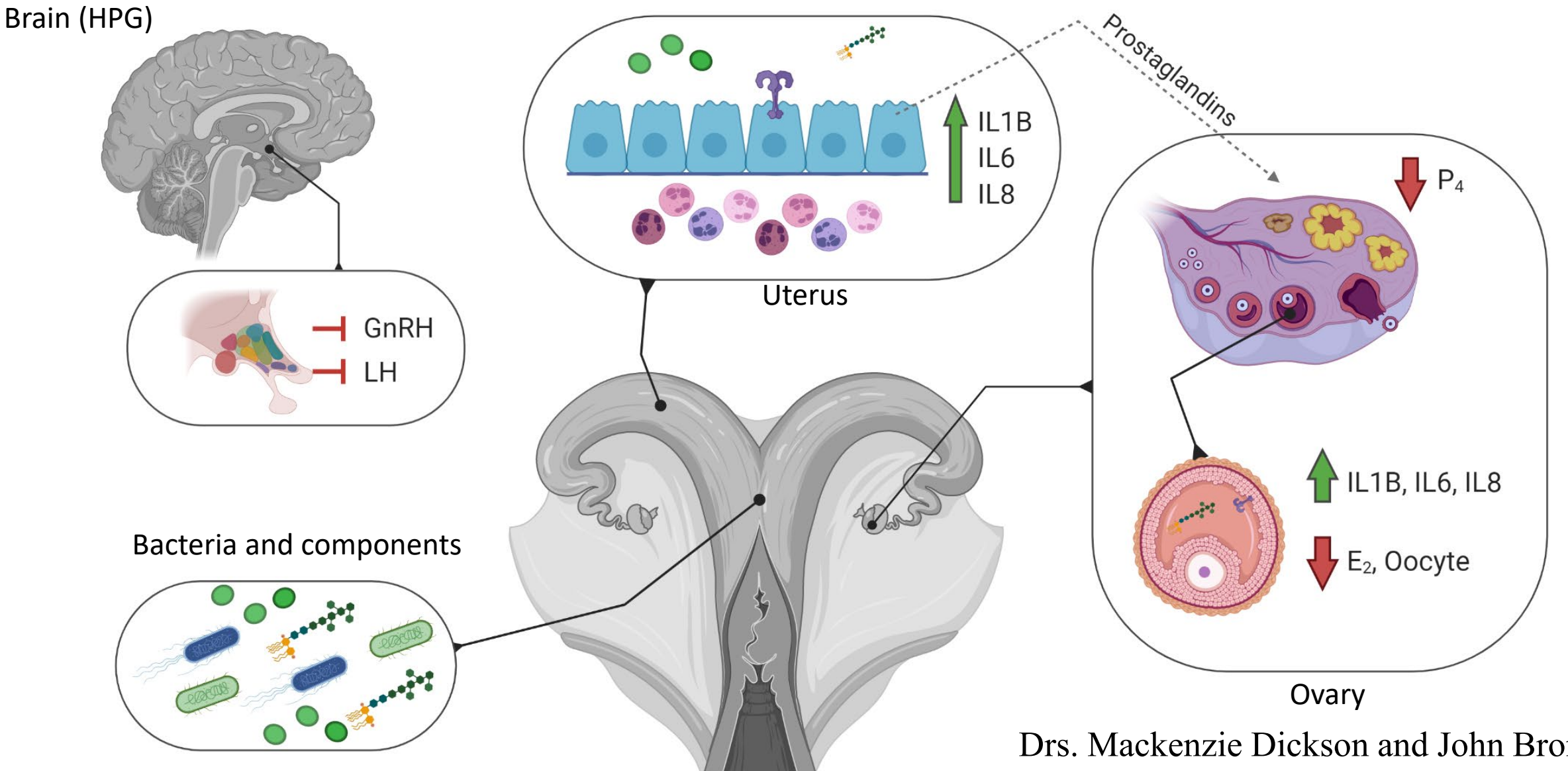


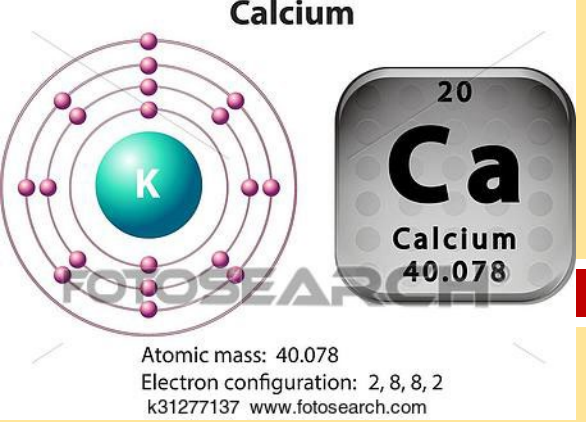
Figure 1 Bacterial translocation is associated with the development of nonalcoholic steatohepatitis. NASH: Nonalcoholic steatohepatitis.

Inflammation and Reproduction?

LPS Negative Effects Repro From Multiple Angles



Drs. Mackenzie Dickson and John Bromfield



https://www.fotosearch.com/CSP142/k31277137/

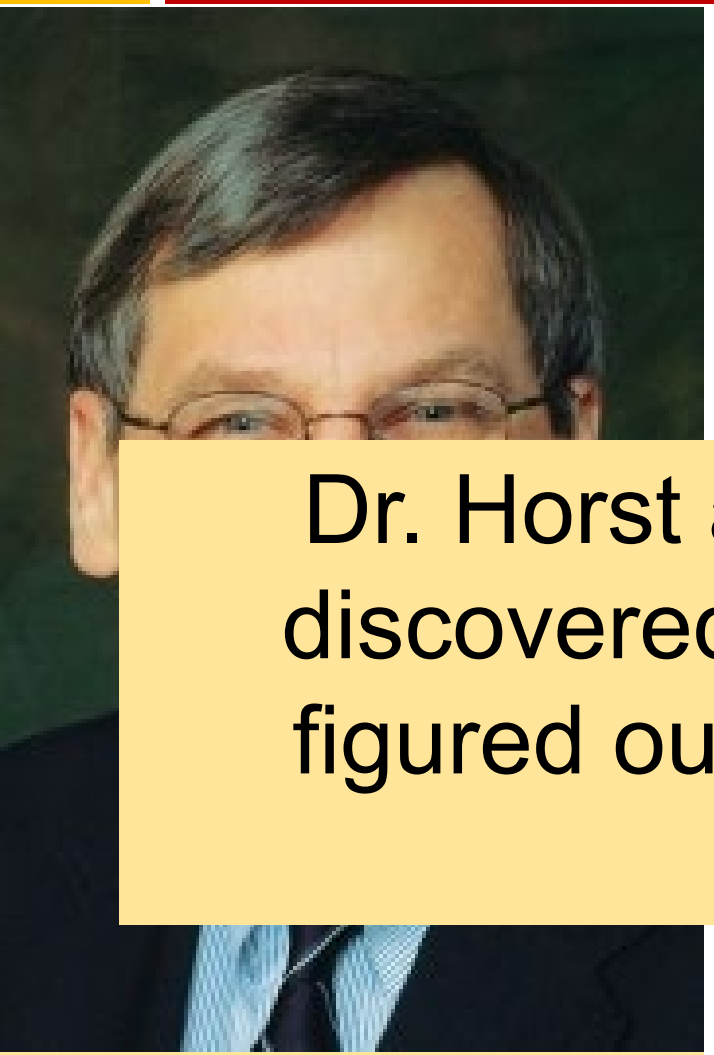
Hypocalcemia Dogma

https://www.farmersjournal.ie/milk-fever-the-problem-of-low-blood-calcium-in-cattle-319488

- Milk uptake of Ca is so quick and extensive that it exceeds the homeostatic capacity to replenish it.

- Academic & Industry Goal: <u>Minimize postcalving hypocalcemia</u>

Dr. Ron L. Horst



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Citations	32723	6863
h-index	94	40
i10-index	342	145

Dr. Horst and his students/collaborators discovered the biology of milk fever AND figured out a prefresh dietary strategy to prevent it

Regulation of Calcium and Phosphorus Homeostasis in the Dairy Cow

RONALD L. HORST
National Animal Disease Center
Agricultural Research Service
US Department of Agriculture
Ames, IA 50010

ABSTRACT

This paper describes the mechanism of calcium and phosphorus homeostasis in dairy cows in an effort to provide a clearer understanding of the rationale behind current management and supplementation practices. Specifically addressed is the need to keep prepartum dietary calcium intake at ⩽ 50 g/d to minimize the incidence of milk fever. Also discussed is the need to increase National Research Council recommendations for postpartum dietary calcium from 2.7 to 3.4 g/kg milk. This is particularly important during the first 1 to 2 mo of lactation to maintain calcium balance.

INTRODUCTION

In common with other homeostatic controls,

from these pools. Regulation of the Ca and P

Received December 3, 1984.

pools are under the influence of two potent calcitropic hormones — parathyroid hormone (PTH) secreted from the parathyroids and 1,25-dihydroxyvitamin D [1,25-$(OH)_2$D], the metabolite of vitamin D produced in the kidney. This paper will describe the nutritional-endocrine interactions involved in the maintenance of Ca and P in plasma.

DISCUSSION

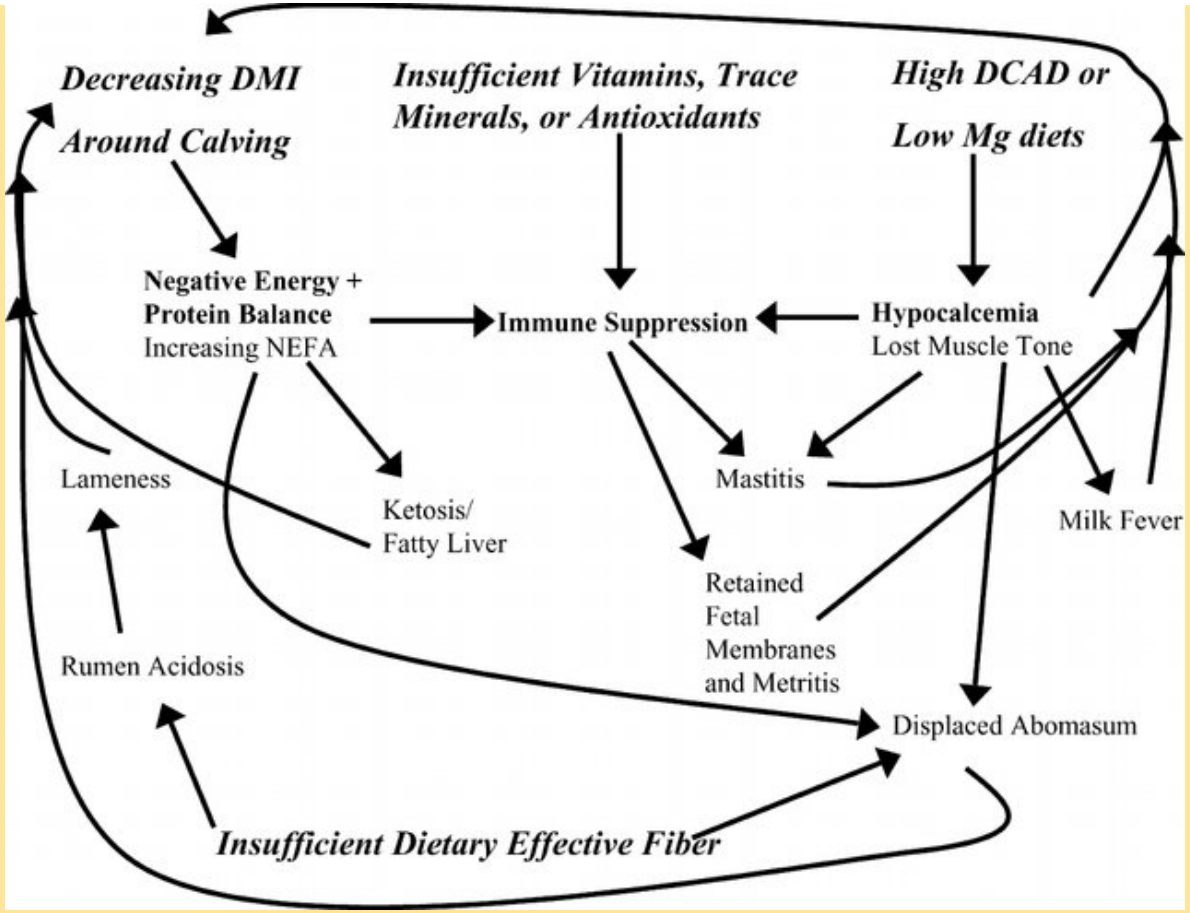
Vitamin D Regulatory System

The two major natural sources of vitamin D to ruminants result from photochemical conversion of 7-dehydrocholesterol to vitamin D_3 in the skin or from plants as a result of photochemical conversion of ergosterol to vitamin D_2. Vitamins D_3 and D_2 also can be supplemented in the ruminant diet by commercially available crystalline forms. Vitamin
rising from photochemical production
skin, enters the extracellular fluid and
es immediately available for further
olism. However, when supplemented
bovine diet, vitamin D metabolism
y begins in the rumen. Recent work in
boratory showed that vitamin D_2 and
n D_3 are converted by microorganisms to
0-keto-19-nor-vitamin D (44). This me-
e may have a role in the in vitro de-
ion of vitamins D_2 and D_3. Its physiologic
ance and biochemical significance are
t understood.
e vitamin D (D_2, D_3, or both) enters the
it circulates at relatively low concen-
s (1 to 3 ng/ml) in cows (29). This
menon is probably a result of its rapid
ulation in the liver. Once in the liver, it is
ted to 25-hydroxyvitamin D (25-OHD) (14). This metabolite is the major circulating form of vitamin D under normal conditions (29). The 25-OHD is converted to several polar metabolites (Table 1). However, of all the vitamin D_2 and D_3 metabolites known, only

Hypocalcemia

- Clinical hypocalcemia (milk fever) needs a pre-calving dietary strategy
  - The marked reduction in clinical milk fever is arguably the biggest advancement in dairy nutrition in the last 40 years
- Clinical hypocalcemia is pathological
  - It warrants immediate intervention
- Is subclinical hypocalcemia pathological?
  - Is it detrimental to health, productivity and profitability?

Morbidity is Sometimes Associated with Subclinical Hypocalcemia



Goff, 2006

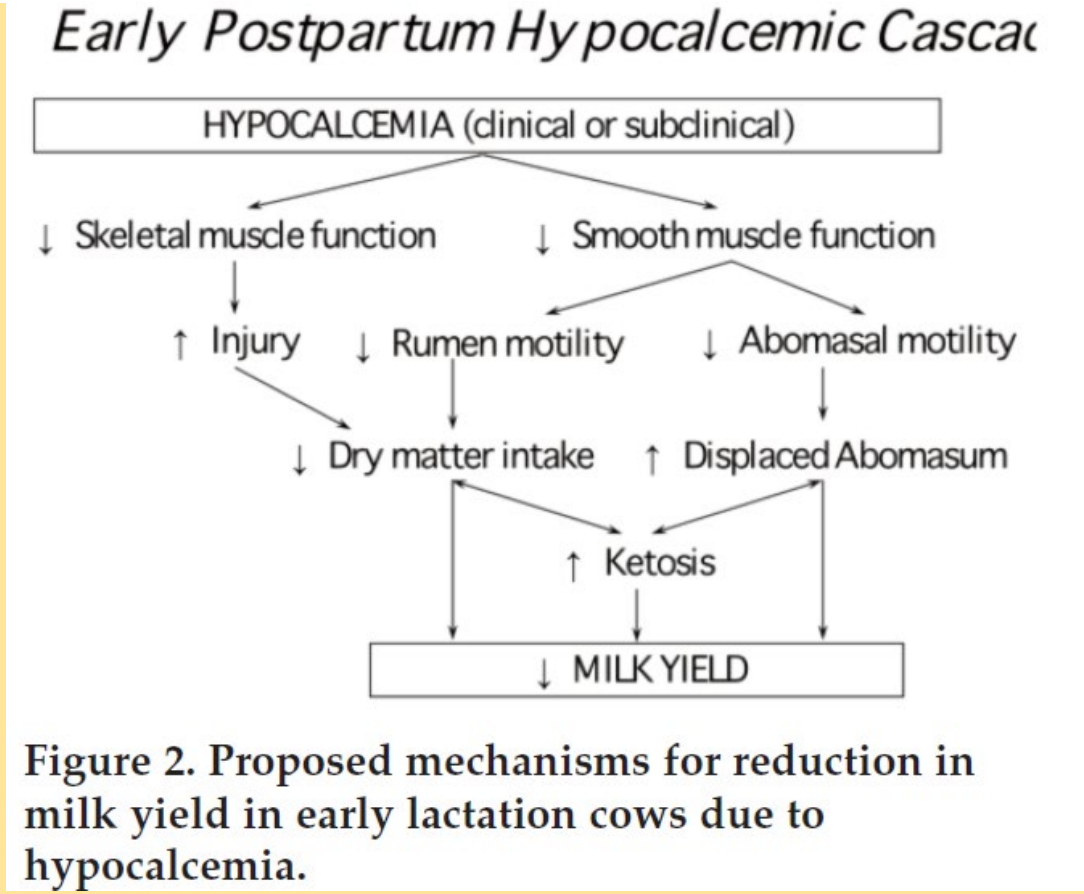


Figure 2. Proposed mechanisms for reduction in milk yield in early lactation cows due to hypocalcemia.

Oetzel, 2012

Reminder: Guiding Concepts and Principles

- The best indicators of “health” are feed intake and milk yield.

J. Dairy Sci. 95:1240–1248
http://dx.doi.org/10.3168/jds.2011-4586

Associations of subclinical hypocalcemia at calving with milk yield, and feeding, drinking, and standing behaviors around parturition in Holstein cows

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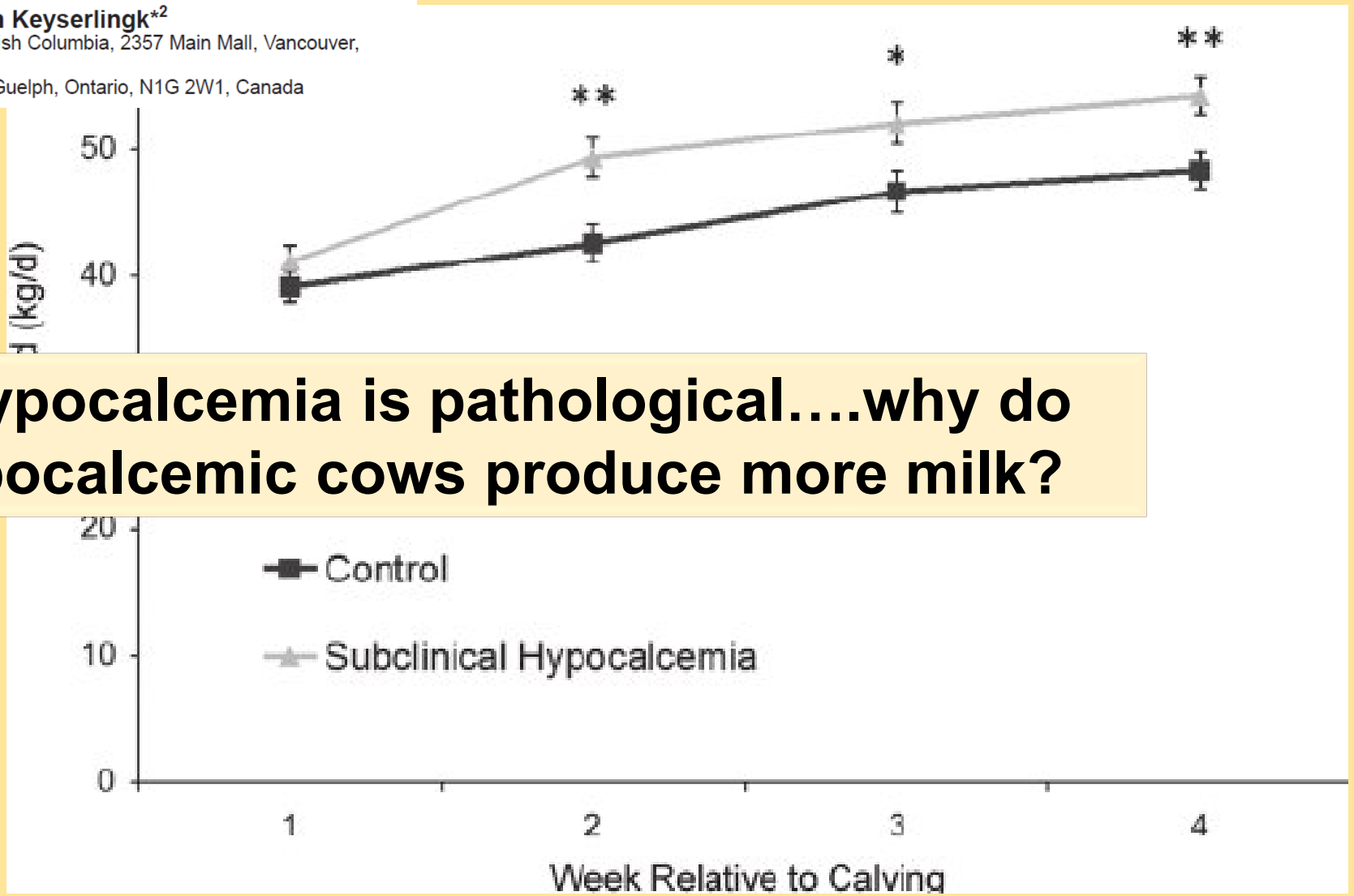
*Animal Welfare Program, Faculty of Land and Food Systems, University of British Columbia, 2357 Main Mall, Vancouver, British Columbia, V6T 1Z4, Canada
†Department of Population Medicine, Ontario Veterinary College, University of Guelph, Ontario, N1G 2W1, Canada



If subclinical hypocalcemia is pathological….why do subclinical hypocalcemic cows produce more milk?

Subclinical hypocalcemia is often associated with <u>increased</u> productivity

Immune activation was identified as a cause of milk fever more than 130 years ago

MILK FEVER (PARTURIENT PARESIS) IN DAIRY COWS—A REVIEW

J. W. HIBBS

Ohio Agricultural Experiment Station, Wooster

Milk fever (parturient paresis) is an afebrile disease which typically is associated with parturition and beginning lactation. It is characterized by a sudden paralysis, gradual loss of consciousness and, if untreated, usually terminates in death. Few diseases of livestock have caused as much theoretical controversy and interest as has milk fever. Gradually, through the years, much has been learned about the nature of milk fever, and effective means of treatment have been devised, resulting in a reduction in mortality of from 60 to 70 per cent to less than 1 per cent. The basic physiological cause of milk fever has yet to be proven. The "parathyroid deficiency (hypocalcemia) theory" of Dryerre and Greig (54) seems to come the nearest of the many theories that have been advanced to accounting for the immediate cause, but many fundamental questions

THE VETERINARY JOURNAL

AND

Annals of Comparative Pathology.

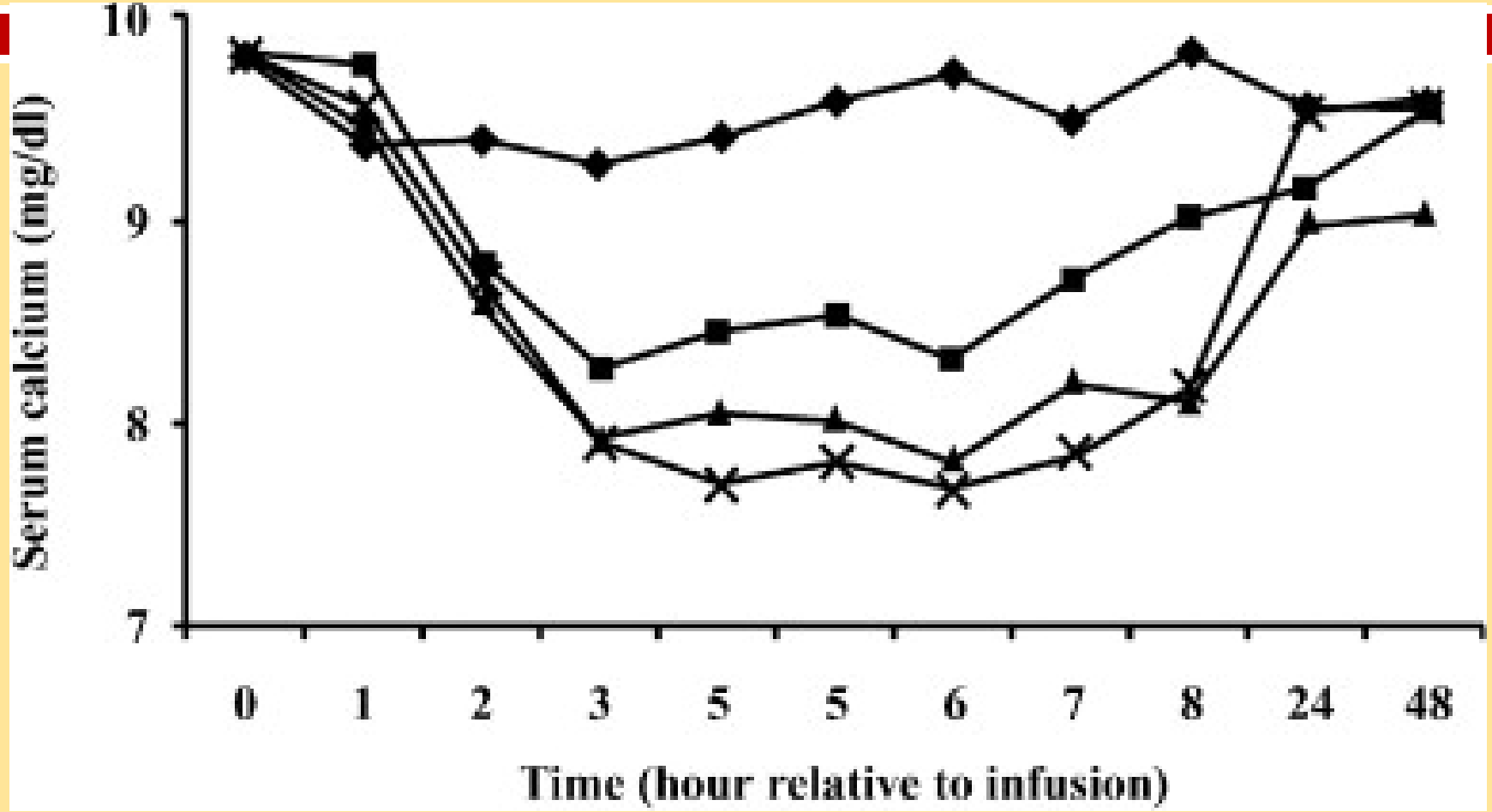
JANUARY, 1889.

PARTURIENT APOPLEXY IN COWS—A FORM OF SEPTICÆMIA.

BY A. HARRISON THOMAS, M.B., C.M., B.SC., ETC., WHITTINGHAM, PRESTON.

LPS administration, mastitis and sepsis all cause severe and acute hypocalcemia

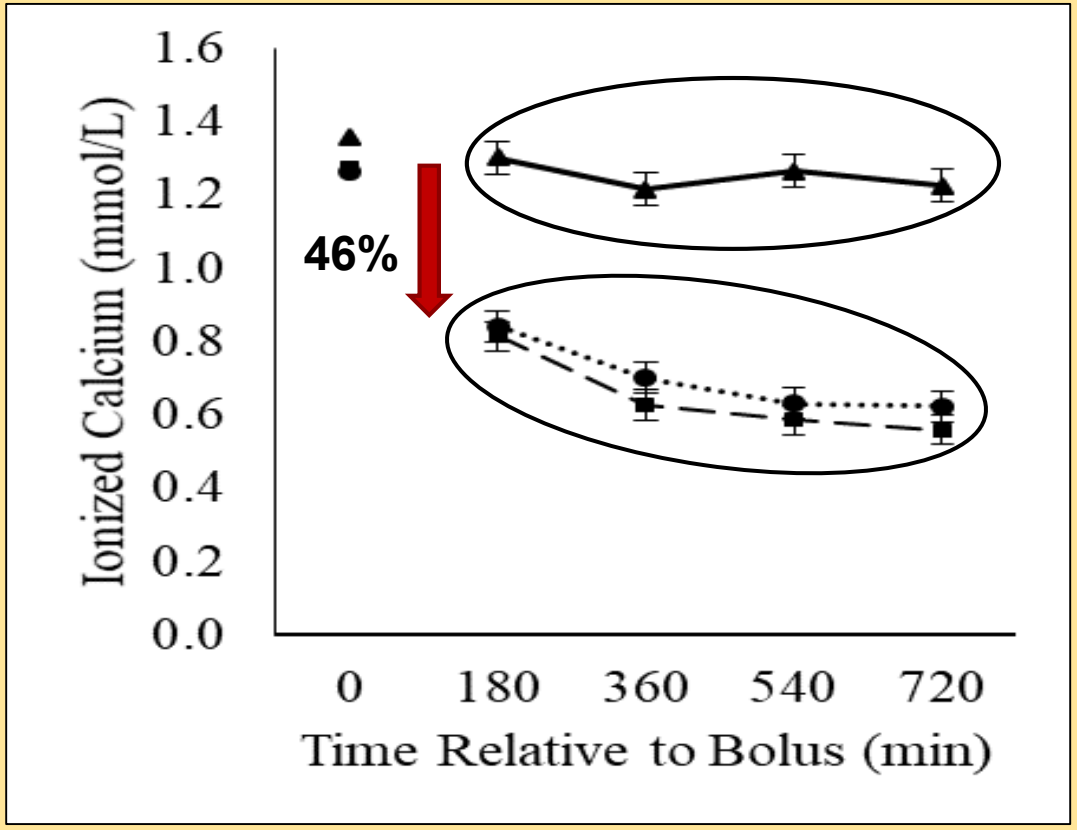
Immune Activation (induced mastitis) Decreases Ca in Dairy Cows



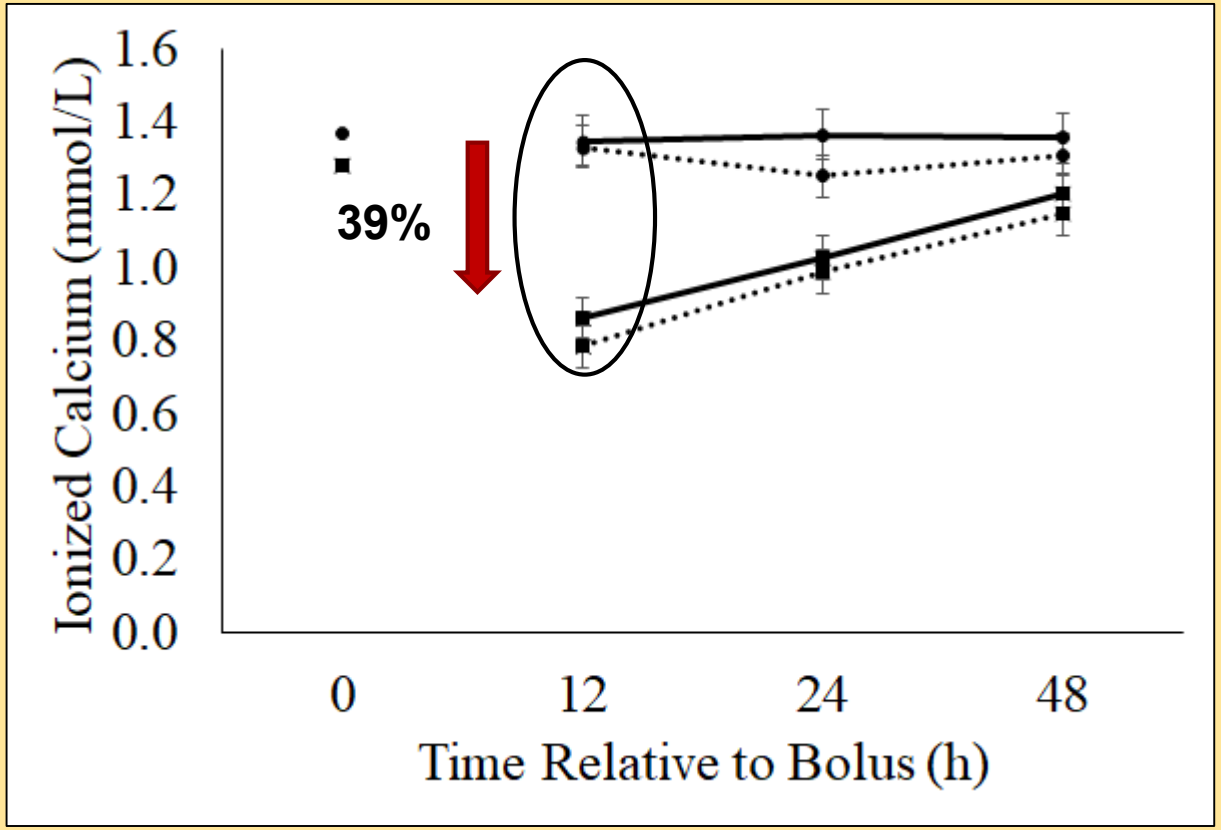
Waldron et al., 2003

I.V. LPS Model

- Immune activation acutely decreases circulating Ca (Kvidera et al., 2017; Horst et al., 2018)



Kvidera et al., 2017



Horst et al., 2018

Immune Activation and Hypocalcemia

- Immune activation causes a marked and unexplainable decrease in ionized Ca
  - Response is conserved across species:
    - (Naylor and Kronfeld, 1986; Elsasser et al., 1996; Carlstedt et al., 2000; Toribio et al., 2005)
  - Paradoxical response as Ca regulates leukocyte activation and function
    - (Hendy and Canaff, 2016)
- Ca administration increases incidences of organ failure and mortality during sepsis
  - Pigs (Calstedt et al., 2000)
  - Humans (Malcolm et al., 1989)
- Hypocalcemia is a protective strategy?
  - Ca interferes with lipoprotein sequestration of endotoxins

LPS detoxification

LPS aggregates (Normocalcemia)

Ca^{2+}

LBP

CD14

Lipoprotein

TLR4

Leukocyte

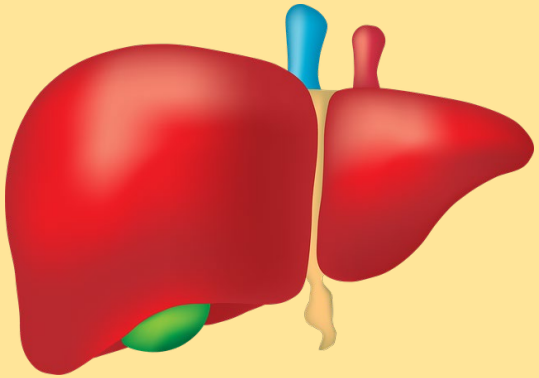
Cytokines

Cytokines

Cytokines

LPS monomers (Hypocalcemia)

Lipoprotein



Immune Activation and Hypocalcemia

- Fact: All transition cows experience some degree of immune activation. Only the magnitude of inflammation differs
- Fact: Immune activation acutely causes hypocalcemia
- **It's reasonable to conclude that immune activation contributes to some types of subclinical hypocalcemia**

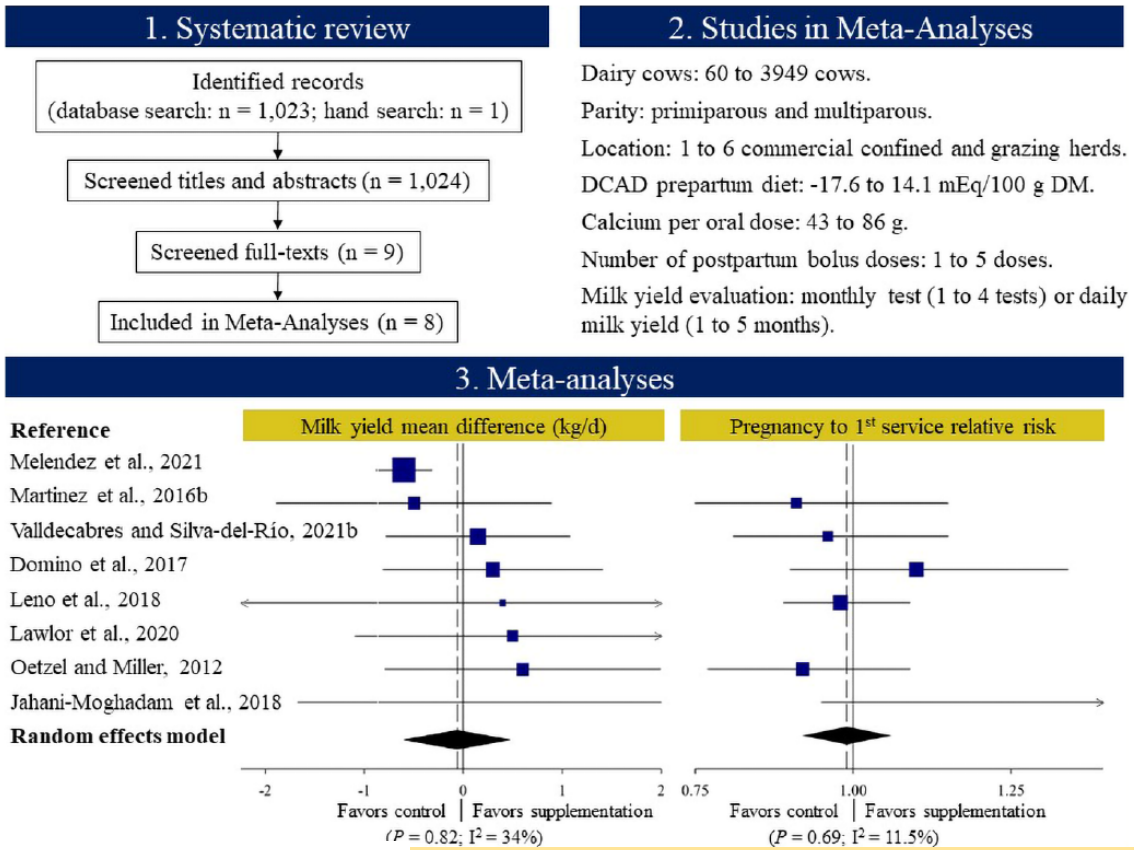
Does intervening and ameliorating subclinical hypocalcemia benefit the cow?

JDS Communications®
2023; 4:9–13

https://doi.org/10.3168/jdsc.2022-0235
Mini-Review
Animal Nutrition and Farm Systems

Production and reproduction responses for dairy cattle supplemented with oral calcium bolus after calving: Systematic review and meta-analysis

Ainhoa Valldecabres,[1,2] Rúbia Branco-Lopes,[2,3] Christian Bernal-Córdoba,[2,3] and Noelia Silva-del-Río[2,3]*



Summary

Meta-analytical methods were used to quantify the associations between prophylactic blanket postpartum oral Ca bolus supplementation and milk yield and risk of pregnancy to first service in dairy cows. Nine relevant studies were identified following a systematic review of the literature published between January 2010 and September 2021. Eight of the eligible studies reported feeding low or negative dietary cation-anion difference diets prepartum. The meta-analyses revealed a lack of evidence for a group level response on milk yield or risk of pregnancy to first service after prophylactic blanket postpartum oral Ca bolus supplementation.

frontiers | Frontiers in Veterinary Science

TYPE Systematic Review
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Effects of oral calcium on reproduction and postpartum health in cattle: a meta-analysis and quality assessment

Zheng-Ren Ma[1], Ling-Li Ma[2], Fei Zhao[3]* and Yan Bo[3]*

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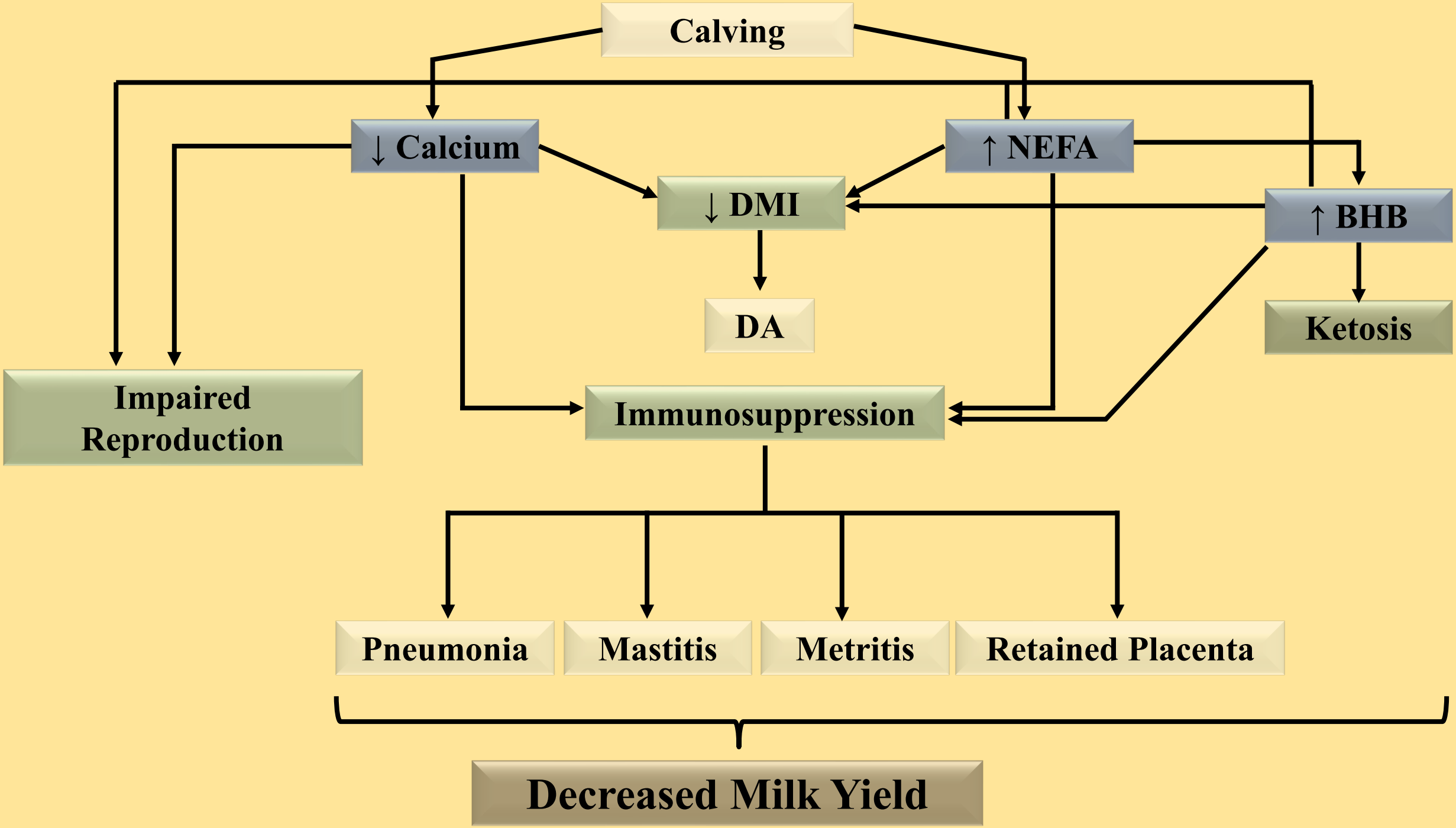
“there is no evidence that oral Ca can reduce the incidence of postpartum metritis, ketosis, mastitis and abomasum displacement, or improve serum Mg/P concentrations, pregnancy risk and milk yield.”

The body of evidence does not support the idea that preventative and prophylactic calcium boluses improve cow health or production

Traditional Belief

Increased NEFA, Hyperketonemia, and Hypocalcemia…..**CAUSE** production and health problems

This is not just an ivory tower debate, it has pragmatic and economic consequences


Calving
↓ Calcium
↑ NEFA
↓ DMI
↑ BHB
DA
Ketosis
Impaired Reproduction
Immunosuppression
Pneumonia
Mastitis
Metritis
Retained Placenta
Decreased Milk Yield

Paradigm Shifting Concept

Increased NEFA and Hyperketonemia are ca d

Low Feed Intake, high NEFA, Hyperketonemia and hypocalcemia are merely SYMPTOMS….a reflection of prior immune stimulation

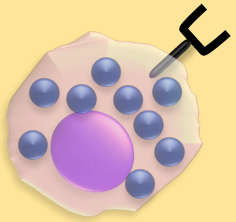
Hypocalcemia is a consequence of immune activation

Mycotoxins

Mastitis

Leaky Gut

Metritis



LPS/Inflammation

Impaired Reproduction

Fatty Liver

↓ DMI

Hypocalcemia

↑ NEFA

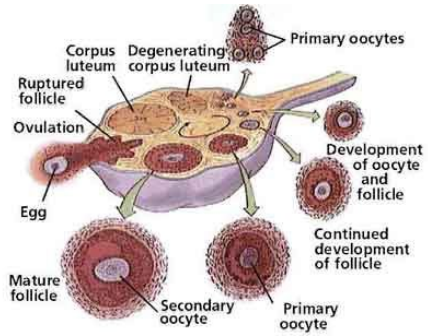
DA

↓ Milk Yield

↑ BHB

Ketosis

Unsuccessful Transition



Fatty Liver, Excessive Ketone Synthesis

Reduced DMI

Adipose

NEFA

Muscle

E

Milk Fat

Liver

Ketone

Rumen

G

C3

LPS

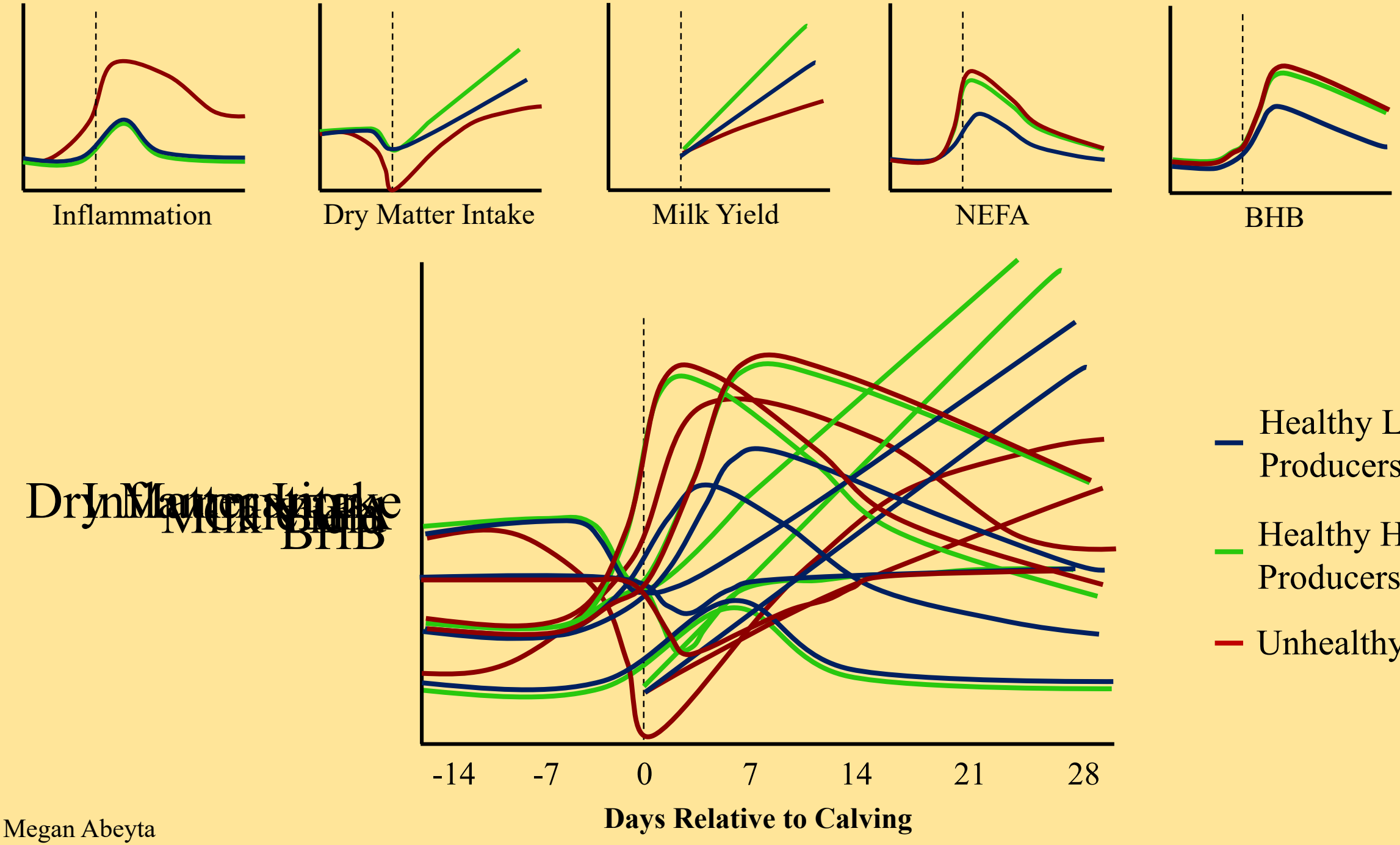
↓ Ca

Mammary Gland

Milk Production

Metabolic Flexibility:
Decreased Insulin Sensitivity
Glucose redirected to immune system

Baumgard and Rhoads, 2013



Dr. Megan Abeyta

Ketosis Scenario

- Two cows in the fresh pen
  - 10 DIM
  - Multiparous

- Both are hyperketonemic (i.e. 1.25 – 2.50 mmol/l)

Ketosis: When (or if) to intervene?

- Treat:
  - High ketones
  - Not coming into milk
  - Not aggressively eating
  - Looks lethargic and melancholic
  - Has a mild fever

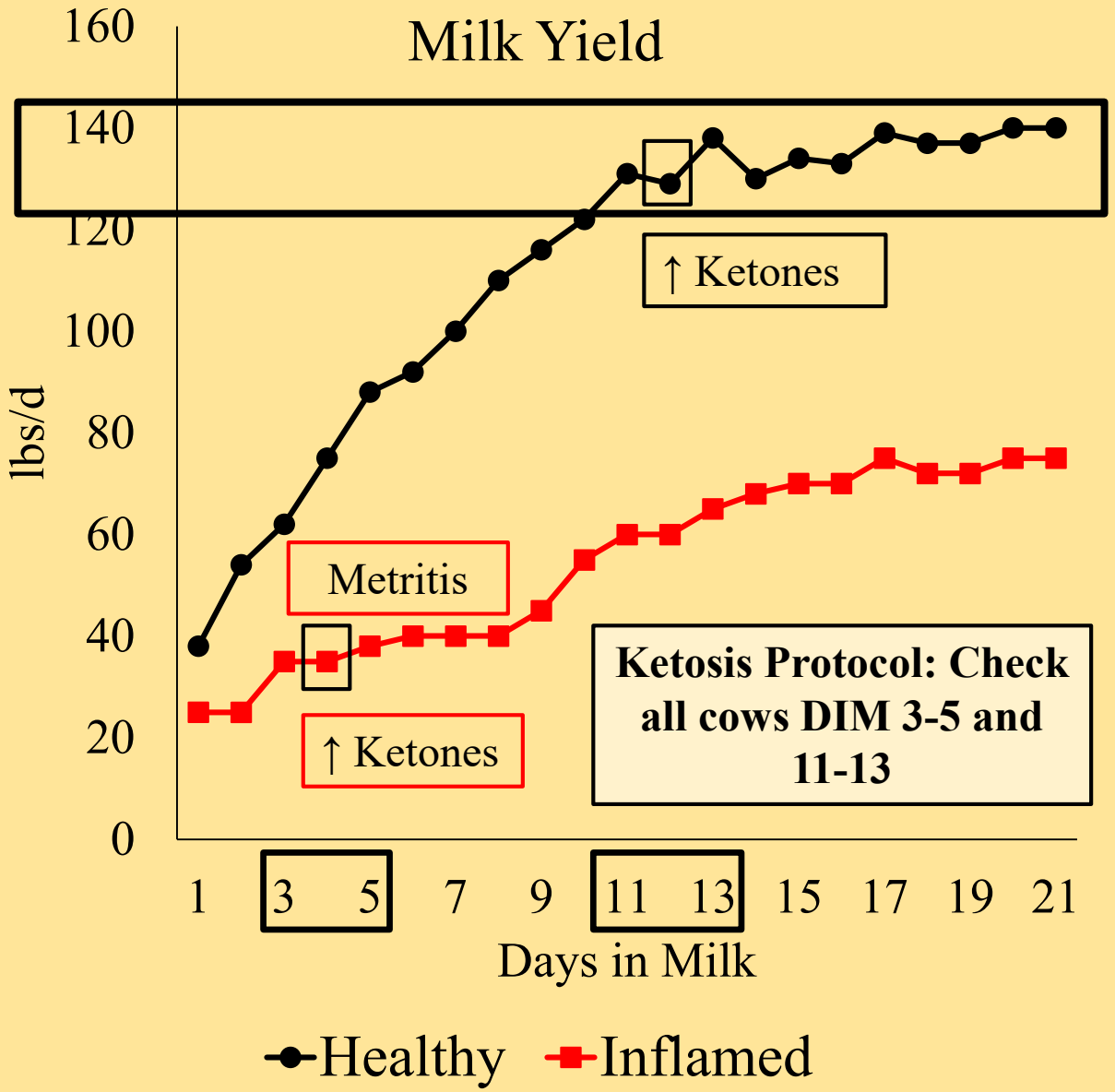
But treating with energy does nothing to address the real problem…..somewhere…..immune-activation is putting the clamp on appetite

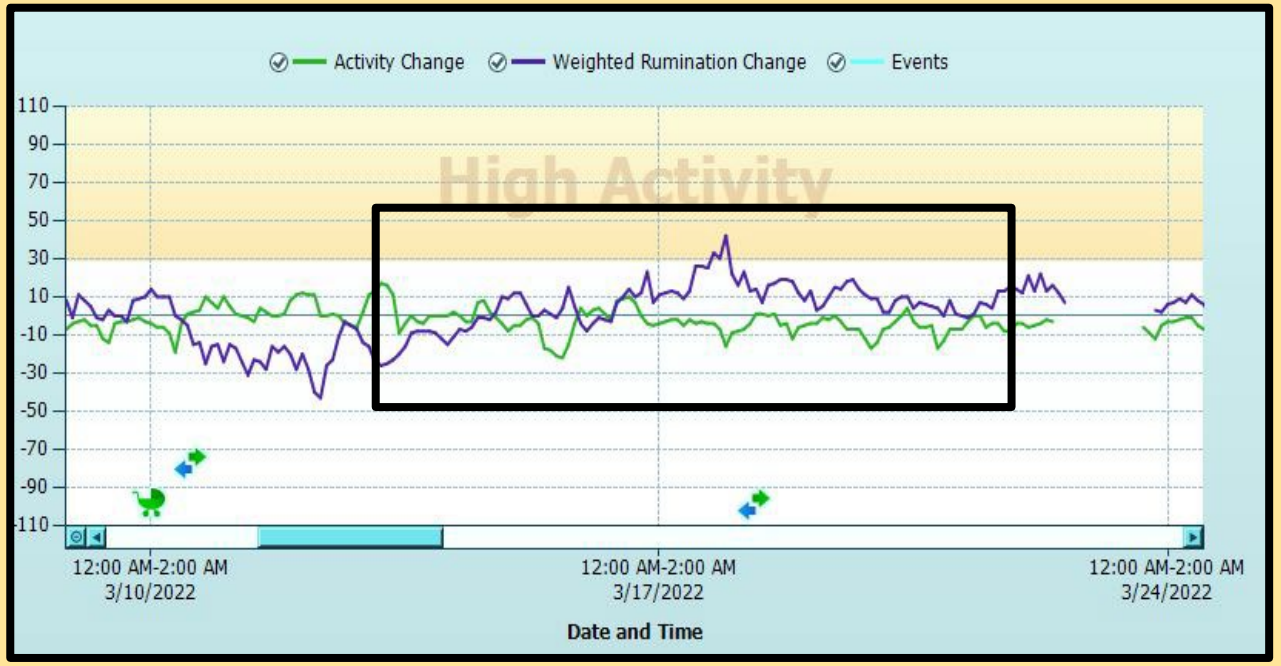
- Don’t mess with
  - High ketones….but she’s eating like a champion
  - Milking like a world-record holder
  - Looks great
  - No fever

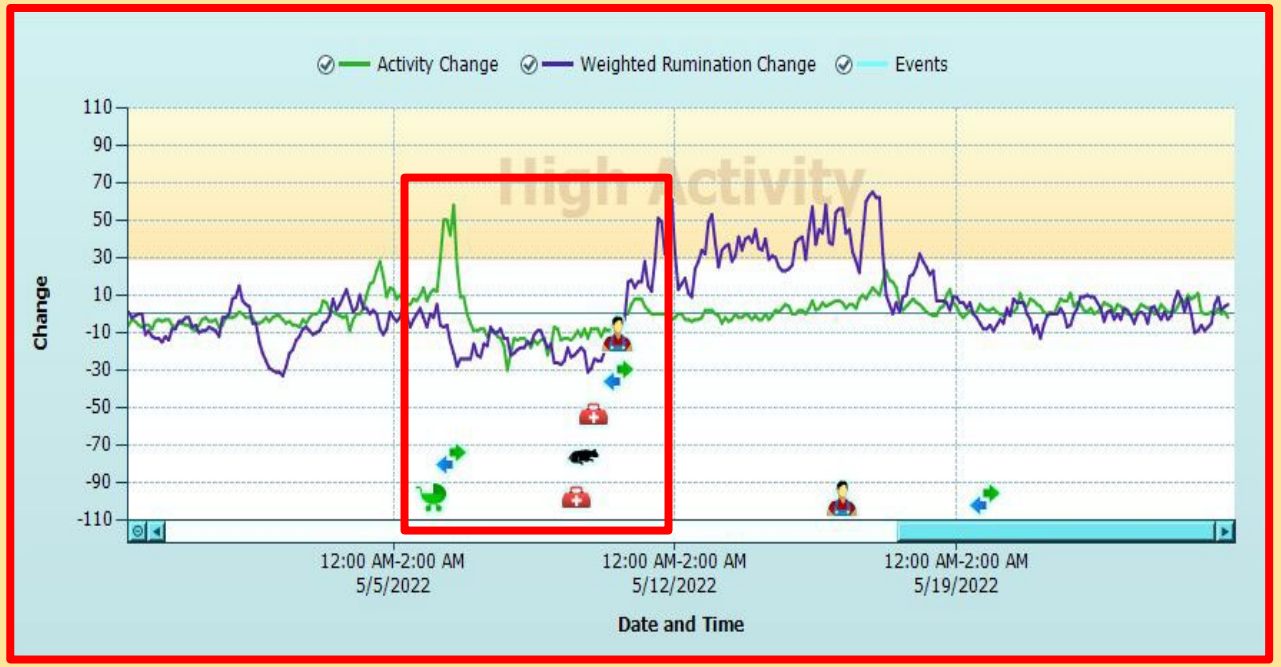
She’s the healthiest cow in the herd

Real World Example

ISU Dairy Farm
Spring of 2022


Milk Yield
160
140
120
100
80
60
40
20
0
lbs/d
↑ Ketones
Metritis
↑ Ketones
Ketosis Protocol: Check all cows DIM 3-5 and 11-13
1
3
5
7
9
11
13
15
17
19
21
Days in Milk
Healthy
Inflamed


Activity Change
Weighted Rumination Change
Events
High Activity
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
12:00 AM-2:00 AM
3/10/2022
12:00 AM-2:00 AM
3/17/2022
12:00 AM-2:00 AM
3/24/2022
Date and Time


Activity Change
Weighted Rumination Change
Events
High Activity
Change
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
12:00 AM-2:00 AM
5/5/2022
12:00 AM-2:00 AM
5/12/2022
12:00 AM-2:00 AM
5/19/2022
Date and Time

Common Critique of My Message

- When PG is given, SHK cows produce more milk
  - McArt et al., 2011
    - 2 out of 3 farms had increased milk yield when SHK cows given PG
  - Lomander et al., 2012
  - Shankare Gowda et al., 2015

- But inconsistent patterns. <u>No effect of PG on milk in SHK cows</u>
  - Bors et al., 2013
  - Ostergaard et al., 2020
  - Capel et al., 2021

J. Dairy Sci. TBC
https://doi.org/10.3168/jds.2024-25208

The effect of monopropylene glycol on milk production, uterine health, and reproductive performance in cows diagnosed with hyperketonemia on 3 pasture-based dairy farms

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

Table 2. Least squares means (SEM) for BCS, BW, and milk yield and component parameters within 15 wk in milk in 735 grazing dairy cows l across 3 dairy farms within New Zealand that tested positive for hyperketonemia (HYK; blood BHB ≥1.2 to 2.9 mmol/L) one or more times wit DIM[1]

	LSM (SEM)		*P*-value[2]		
Variable	Control	MPG	Timing of first HYK positive test	Treatment	Treatment × w
BCS[3] (10-point scale), units	4.35 (0.02)	4.36 (0.02)	0.52	0.83	0.33
BW,[3] kg	474 (2.09)	472 (2.11)	0.01	0.26	0.63
Milk yield, kg/d	23.2 (0.25)	23.0 (0.25)	0.11	0.38	0.39
ECM yield, kg/d	25.1 (0.24)	24.7 (0.24)	0.57	0.06	0.90
Fat yield, kg/d	1.05 (0.01)	1.03 (0.01)	0.91	0.01	0.95
CP yield, kg/d	0.85 (0.01)	0.84 (0.01)	0.31	0.21	0.52
Fat, %	4.52 (0.03)	4.46 (0.03)	0.33	0.05	0.78
CP, %	3.66 (0.02)	3.64 (0.02)	0.13	0.42	0.84

[1]Cows were assigned to treatment with nonintervention control (n = 356) or monopropylene glycol (MPG; n = 379) treatment groups. Models in calving season day within farm, age, and blood BHB concentration at first HYK positive test
[2]Week was statistically significant at $P < 0.001$ for all outcomes due to overall temporal effects.
[3]Overall mean BW and BCS during the first 15 wk postcalving.
[4]Mean daily milk and ECM yield and components during the first 15 wk in milk.

PG significantly decreased ECM

CONCLUSIONS

To our knowledge, no other randomized controlled trial has tested cows for HYK up to 15 times within the first 35 DIM, and subsequently, treated half of those cows with MPG. This may, therefore, be the most comprehensive treatment-based study for HYK to date, and was undertaken in grazing dairy cows. The results indicate that administering MPG in grazing dairy cows with HYK can help cows resolve HYK (i.e., reduce blood BHB concentrations) and reduce the likelihood of Sev-HYK. The lack of positive effects of MPG treatment on other economically important traits (e.g., milk production, uterine health, and reproductive performance) in HYK cows, however, indicates there would be little benefit to routine administration of MPG to HYK cows on pasture-based dairy farms based on a blood BHB threshold of ≥1.2 mmol/L.

The body of evidence does not support the prophylactic practice of giving subclinical hyperketonemic cows PG

I’m not even convinced that therapeutic PG administration helps acute ketotic cows

Management Changes?

The nutritionist is rarely to blame for transition cows problems.

High production can only occur in the absence of stress and morbidity

- Instead pay more attention to feed intake (rumination/activity) and milk yield

Immune Activation Causes Inflammation

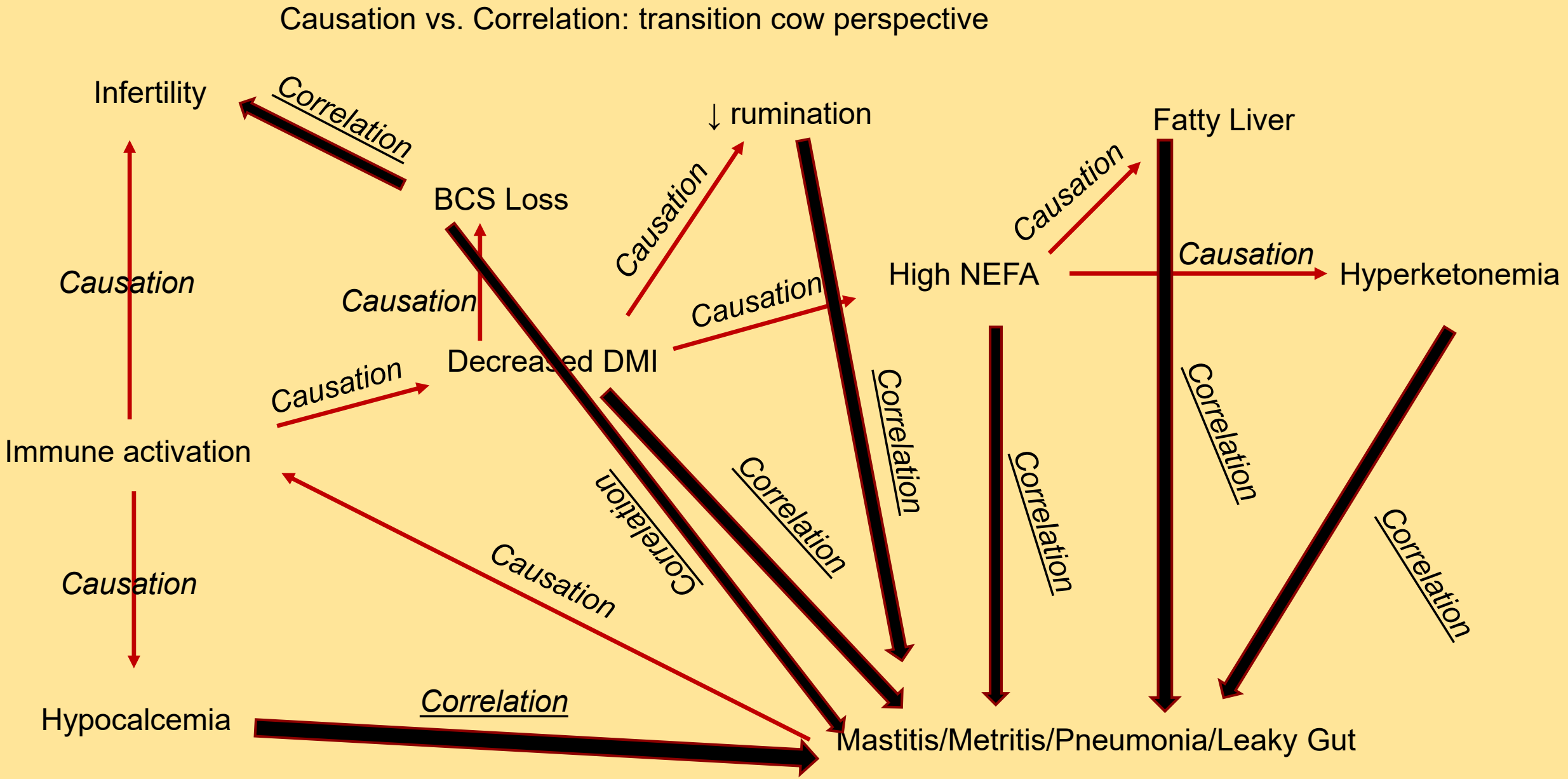
- All transition cows are inflamed (just the magnitude differs)
- Inflammation appears before clinical disease (metritis, mastitis, “ketosis”)
- The immune system “pumps the brake” on feed intake
  - It’s clearly not the only reason for subclinical hypocalcemia
- LPS causes infertility
- Immune activation reduces feed intake
  - It’s the simplest and most logical explanation for why some cows don’t eat well following calving

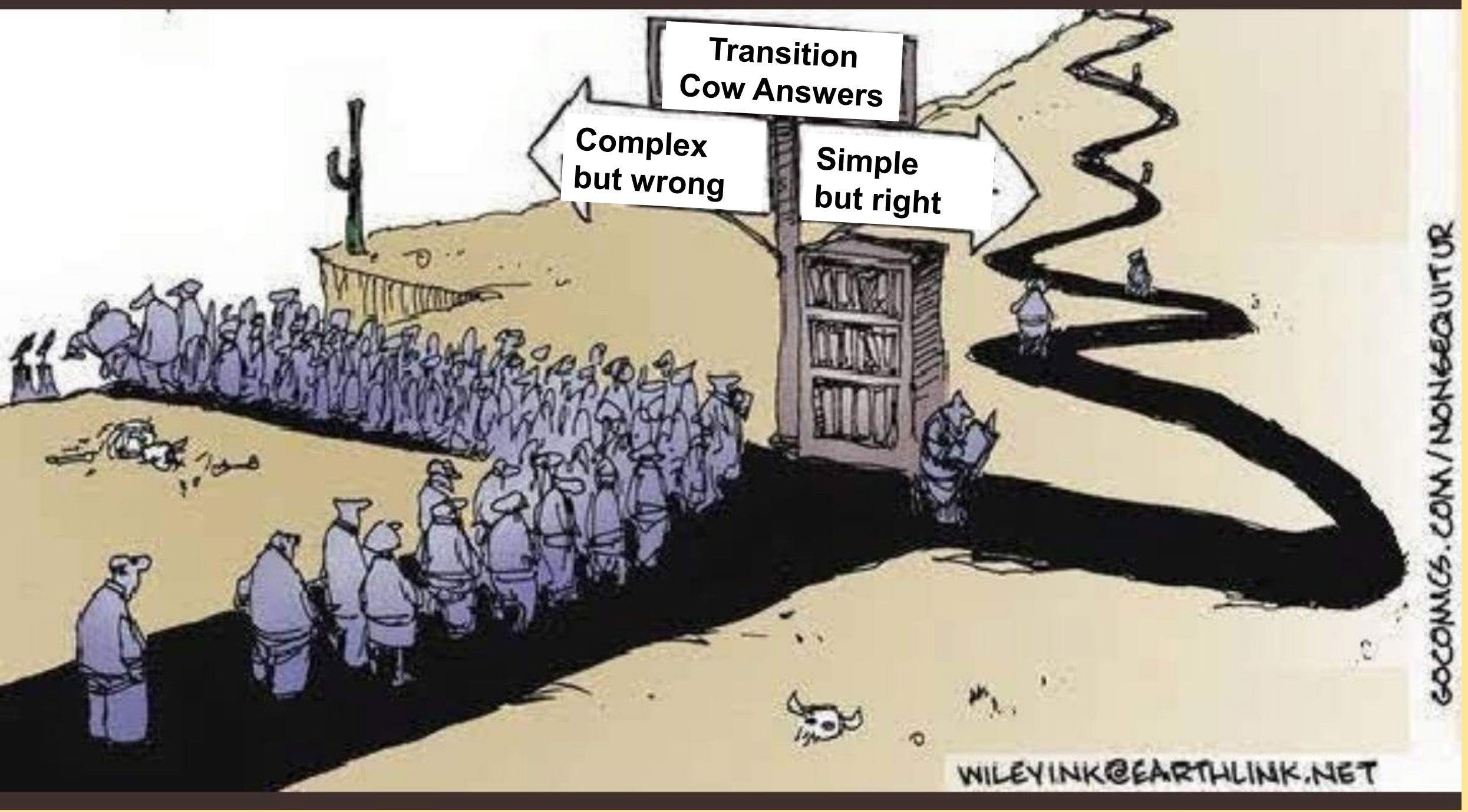
Summary: Inflammation and the Transition Period

- These metabolic and mineral changes are not “dysfunctional”
- They are required to prioritize survival or required for maximum productivity
  - They aren’t to blame (they’re not the cause) for poor productivity
- Our efforts should be in preventing immune activation in the first place

Profitable Production is a Consequence of Wellness

  - Hygiene
    - Minimize environmental pathogens (dry off procedure, dry environment, etc.)
    - Pen cleanliness
  - Dietary strategies
    - Feed hygiene/pathogen binding
    - Prevent GIT disturbances
    - Target molecules aimed and minimizing leaky gut
    - Immune modulation


Causation vs. Correlation: transition cow perspective
Infertility
Correlation
↓ rumination
Fatty Liver
BCS Loss
Causation
Causation
Causation
High NEFA
Causation
Hyperketonemia
Causation
Causation
Decreased DMI
Causation
Correlation
Correlation
Correlation
Correlation
Correlation
Immune activation
Causation
Causation
Correlation
Hypocalcemia
Mastitis/Metritis/Pneumonia/Leaky Gut


Transition
Cow Answers
Complex
but wrong
Simple
but right
WILEYINK@EARTHLINK.NET
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Acknowledgments

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- USDA NRI/AFRI/NIFA
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  - # 2014-67015-21627
  - # 2015- 10843
  - # 2017- 05931
  - # 2017- 10843
  - # 2019- 07859
  - # 2020- 02716
  - # 2021- 09507

Industry Partners

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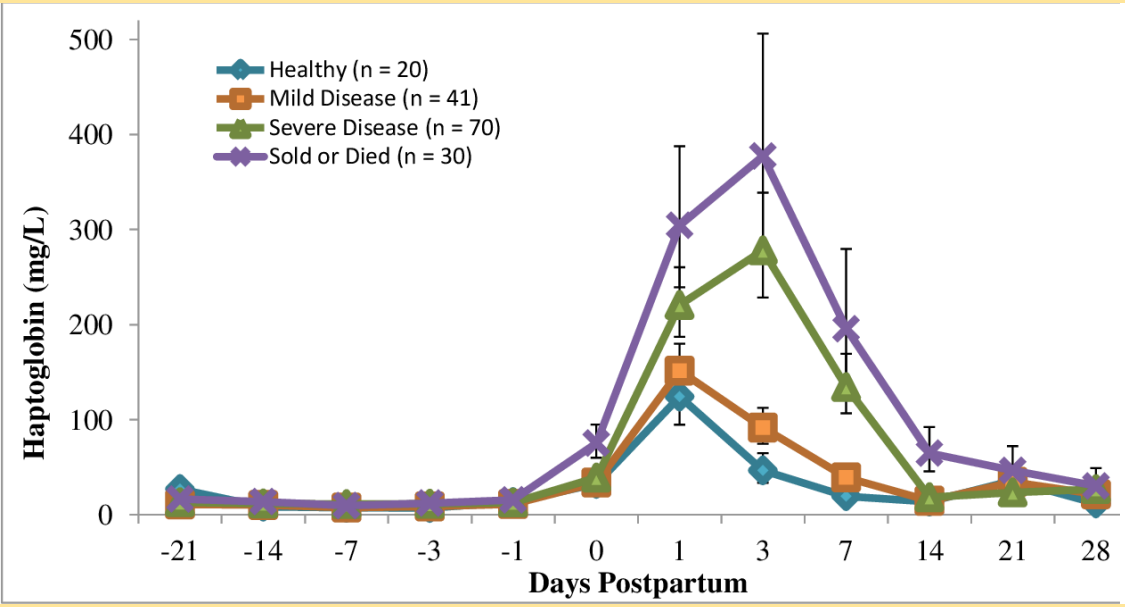
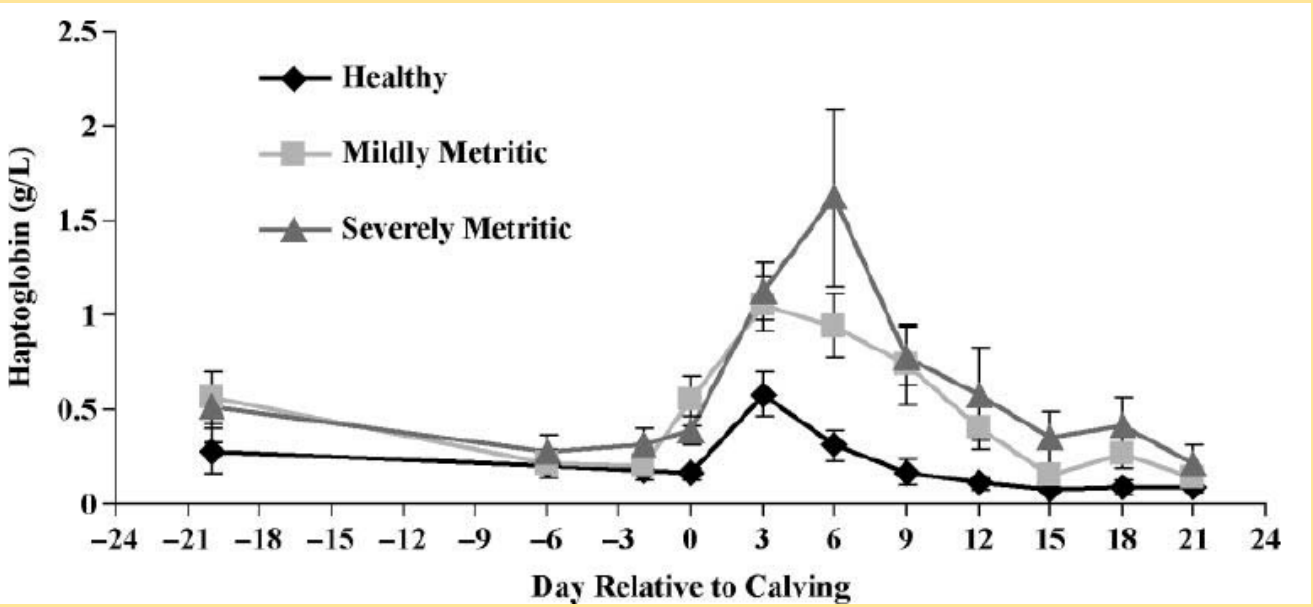
Immune Activation (Haptoglobin) Precedes Clinical Disease

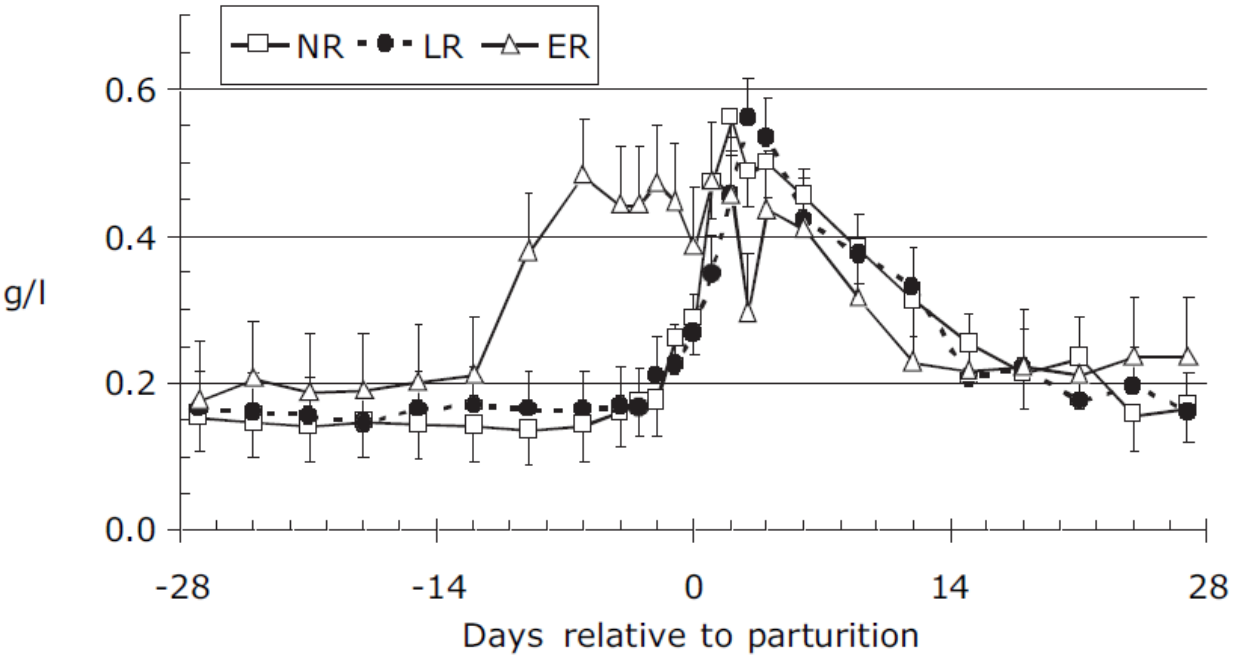


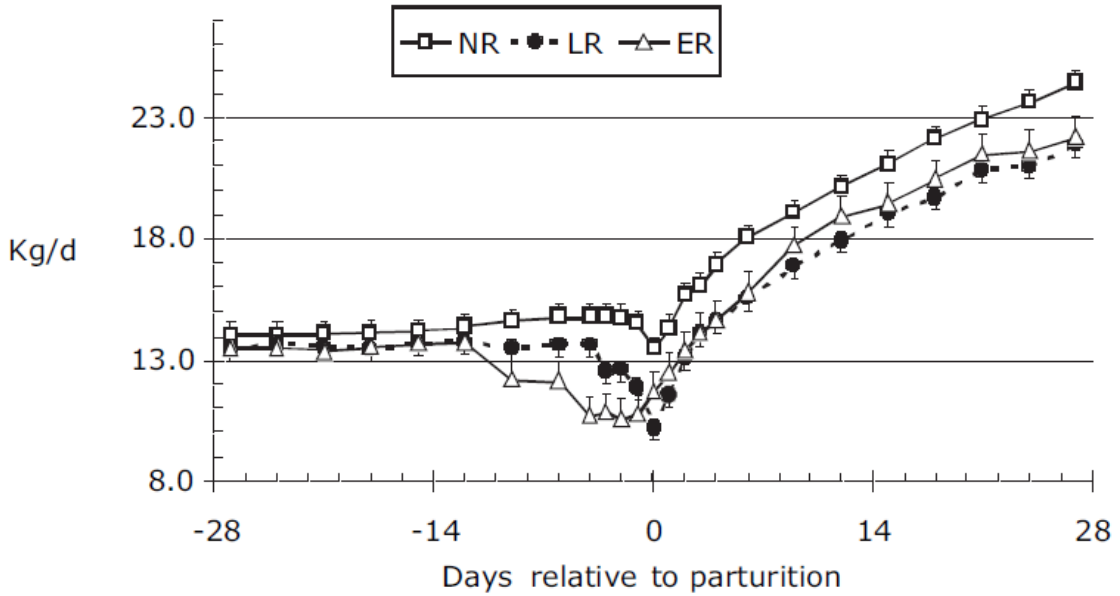
Sebedra 2012



Huzzey et al., 2012

Increased Haptoglobin Mirrors the Decreased DMI





Bertoni et al., 2009

animals 2024 MDPI

Review

Periparturient Mineral Metabolism: Implications to Health and Productivity

Achilles Vieira-Neto [1], Ian J. Lean [2,3] and José Eduardo P. Santos [1,4,*]

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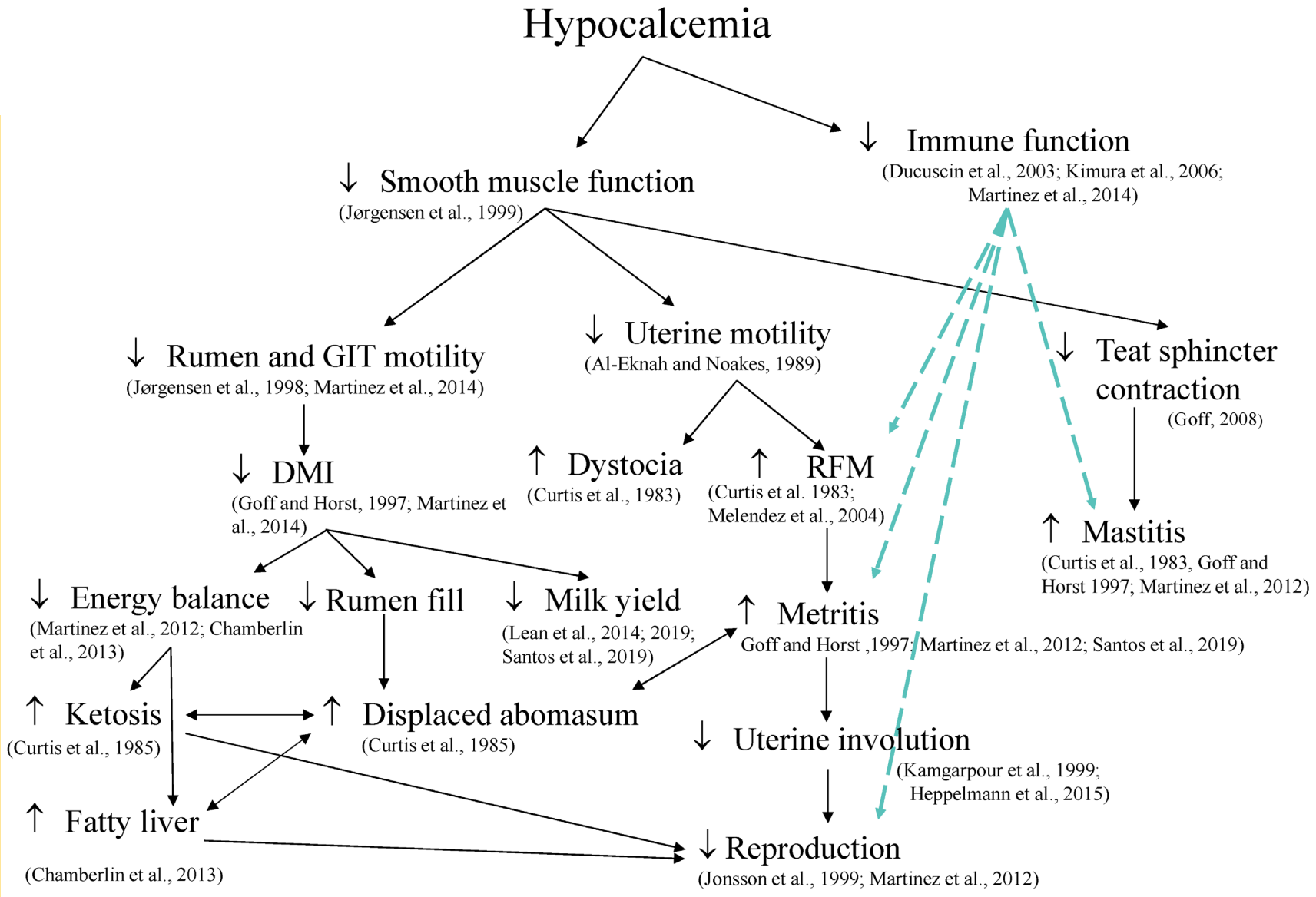

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OUR SPECIALISTS HOW WE CAN HELP PRODUCTS X-ZELIT NEWSROOM ABOUT US CONTACT US MAIZE MASTERCLASS

Newsroom

Home › Newsroom › Latest news from Advanced Nutrition › Subclinical milk fever - the hidden killer?

Subclinical milk fever - the hidden killer?

On average in the UK, subclinical milk fever is affecting up to 75% of the herd. It's unrecognisable and generally remains untreated, as a consequence it's the gateway to other metabolic diseases and ultimately an early cull cow.

Testimonials

"Since working with Advanced Robot, milk yield increased significantly from 29 to 35 kilograms, but milk solids have also been sustained at 4.6% butterfat and 3.4% protein, with total milk solids at 2.73 kilograms sold."

That's not all. Cows suffering from milk fever are between four and nine times more likely to suffer from a miscellany of other metabolic orders, many of which are related to each other. They each come with a significant price tag not only in treatment and vet costs, but also with losses from future milk and fertility delays. Cow suffering milk fever are likely to have increased risks:

- 9-fold increase in the incidence of ketosis in cattle
- 6 times more dystocia/ calving difficulties
- 4-fold increase in the incidence of left displaced abomasum
- 4 times more cases of retained placenta

Even a slight reduction from normal calcium levels can significantly impact production and profitability. A small decrease in blood calcium can increase the risk of:

- Displaced abomasum
- Lower milk production
- Reduce reproductive performance
- A negative energy balance