Epidemiology of Pregnancy Losses and Practical Strategies for Prevention

Klibs N.A. Galvão and Jose E. P. Santos
College of Veterinary Medicine
University of Florida
galvaok@ufl.edu

UF | College of Veterinary Medicine
UNIVERSITY of FLORIDA

UF | UNIVERSITY of FLORIDA
IFAS

Outline

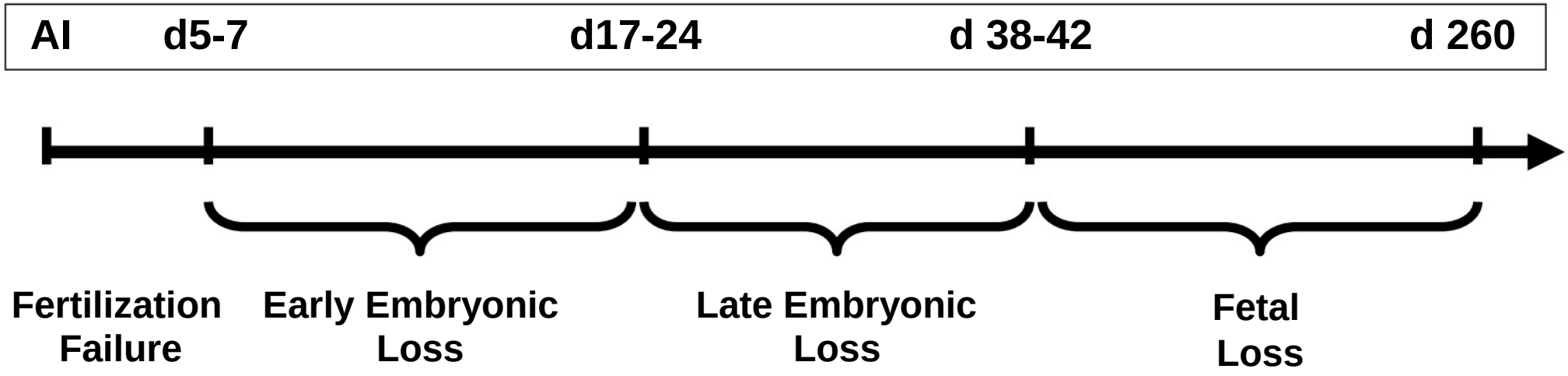
- Importance of pregnancy losses
- Outline the critical period for pregnancy losses
- Main risk factors
  - **Postpartum diseases**
  - Heat stress
  - Anovulation/Low P4 during ovulatory follicle growth
  - Prolonged periods of ovulatory follicle dominance
  - Toxins (gossypol, mycotoxins)
  - Infectious diseases (Neospora, Lepto, BVD, IBR)
- Conclusions

Importance of Pregnancy and Pregnancy loss

- Each new pregnancy costs ~ $278 ($-14 to $551); cow 500 DIM 90 lbs
- Each pregnancy lost costs ~ $555 ($-3 to $1,373)

Reproductive Failure

- Fertilization failure
- Pregnancy loss



Adapted from Santos *et al.,* 2004; ARS

Fertilization and Viable Embryos

Fertilization rate and embryo quality in non-superovulated lactating and nonlactating dairy cattle

Dairy cattle	Method of collection	Number of structures	Days after AI	Fertilization (%)	Viable embryo,[a]		Reference
					Fertilized (%)	Total (%)	
Lactating							
Cows	Uterine flush	38	6	55.3	33.3	18.4	Sartori et al. (2002)
Cows	Uterine flush	41	6	87.8	52.8	46.4	Sartori et al. (2002)
Cows	Uterine flush	45	5	73.3	78.8	57.8	Cerri et al. (in press)
Cows	Uterine flush	41	5	87.2	85.3	74.4	Cerri et al. (in press)
Overall	Uterine flush	165	5–6	76.2 (55.3–87.8)	65.6 (33.3–85.3)	50.0 (18.4–74.4)	
Nonlactating							
Cows	Uterine flush	38	6	89.5	82.3	73.7	Sartori et al. (2002)
Cows	Uterine flush	39	6–7	67.0	93.0	62.3	Dalton et al. (2001)
Cows	Uterine flush	39	6–7	79.0	90.0	71.1	Dalton et al. (2001)
Cows	Uterine flush	37	6–7	98.0	89.0	87.2	Dalton et al. (2001)
Cows	Uterine flush	39	6–7	66.0	92.0	60.7	Dalton et al. (2001)
Cows	Uterine flush	39	6–7	74.0	90.0	66.6	Dalton et al. (2001)
Cows	Uterine flush	39	6–7	82.0	66.0	54.1	Dalton et al. (2001)
Cows	Uterine flush	26	6	81.0	N/A[b]	N/A	DeJarnette et al. (1992)
Cows	Uterine flush	24	6	83.0	N/A	N/A	DeJarnette et al. (1992)
Cows	Uterine flush	19	6	68.0	57.1	36.3	DeJarnette et al. (1992)
Cows	Uterine flush	19	6	58.0			DeJarnette et al. (1992)
Cows	Uterine flush	20	6	70.0	90.3	65.1	DeJarnette et al. (1992)
Cows	Uterine flush	23	6	74.0			DeJarnette et al. (1992)
Cows	Uterine flush	21	6	90.0	94.7	85.2	DeJarnette et al. (1992)
Cows	Uterine flush	22	6	77.0	76.5	58.9	DeJarnette et al. (1992)
Overall	Uterine flush	444	6–7	78.1 (58.0–98.0)	74.1 (57.1–94.7)	57.9 (36.3–87.2)	
Heifers	Uterine flush	32	6	100.0	71.9	71.9	Sartori et al. (2002)

Santos *et al.,* 2004; ARS

Late Embryonic Loss

Late embryonic mortality in lactating dairy cows

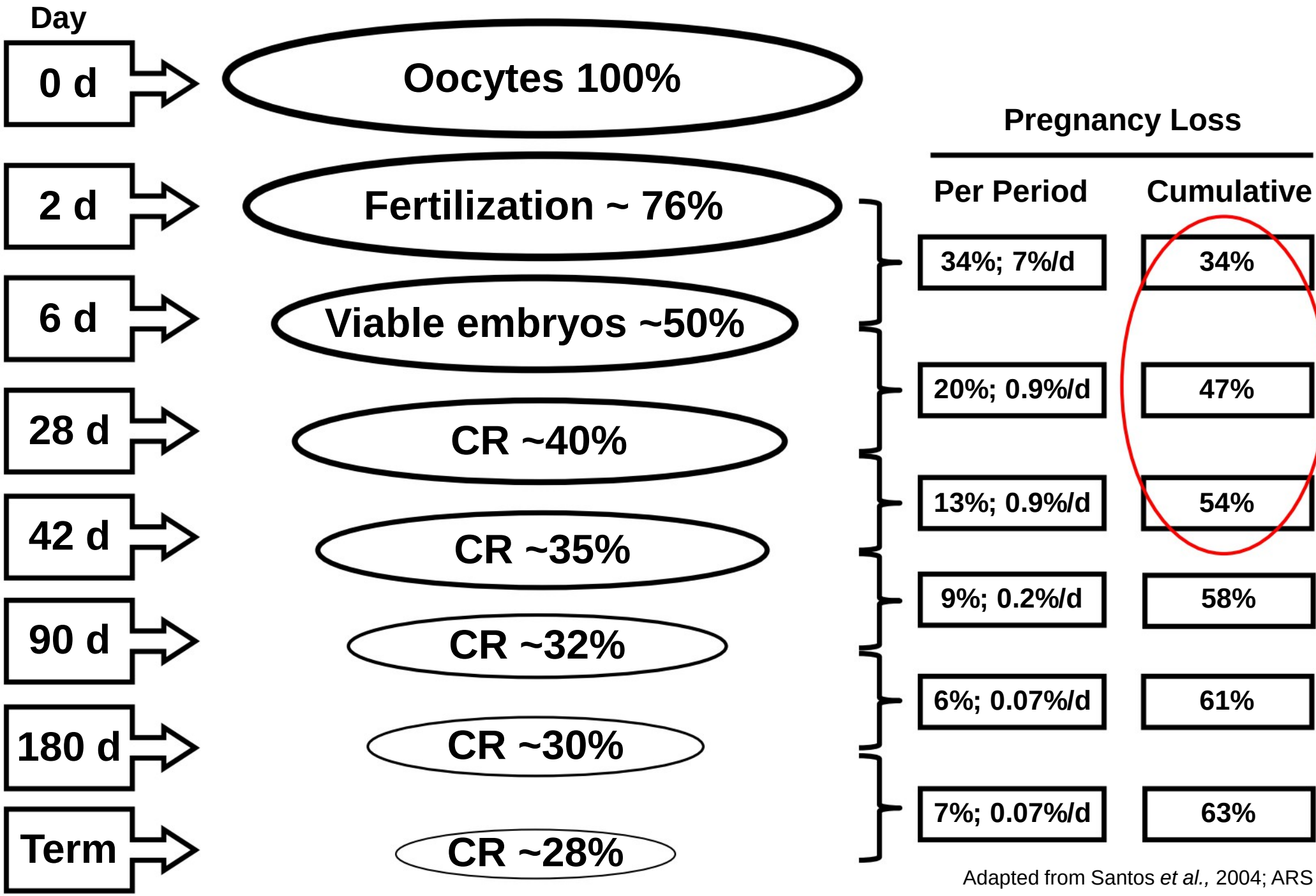
No. of pregnancies	Days of gestation at diagnosis					
	First	Second	Interval (days)	Pregnancy loss (%)	Pregnancy loss (% per day)	Reference
256	28	38–58	~20	28.0	1.40	Cartmill et al. (2001a)
110	27–30	40–50	~16	42.7	2.67	Cartmill et al. (2001b)
261	30	44	14	12.5	0.89	Cerri et al. (2003)
195	28	42	14	17.9	1.28	Chebel et al. (2003a)
74	31	45	14	10.8	0.77	Chebel et al. (2003b)
1465	31	45	14	12.5	0.89	Chebel et al. (in press)
251	27	41	14	17.5	1.25	Galvão et al. (in press)
167	28	39	11	11.4	1.04	Juchem et al. (2002)
139	27	45	18	20.7	1.15	Moreira et al. (2001)
172	28	45	17	9.3	0.55	Santos et al. (2001)
372	31	45	14	11.4	0.82	Santos et al. (2004a)
215	27	41	14	9.9	0.71	Santos et al. (2004c)
705	28	42	14	3.2	0.23	Silke et al. (2002)
488	28	42	14	10.5	0.75	Vasconcelos et al. (1997)
Overall: 4870	27–31	38–50	~15	12.8	0.85	
				(3.2–42.7)	(0.23–2.67)	

Santos *et al.,* 2004; ARS

Late Embryonic and Fetal Loss

Late embryonic and fetal losses in lactating dairy cows and primigravid dairy heifers

Number of pregnancies	Days of gestation at diagnosis				
	First	Second	Interval (days)	Pregnancy loss (%)	Reference
Lactating cows					
1547	35–48	180	~139	9.9	Ettema and Santos (in press)
89	28	56	28	13.5	Fricke et al. (1998)
86	28	64	36	12.8	Gümen et al. (2003)
601	38–44	90–96	~52	10.7	López-Gatius et al. (2002)
3162	41	120–150	~84	9.6	Labèrnia et al. (1996)
285	25–35	Term	~250	22.0	Pursley et al. (1998)
156	45	90	45	8.3	Santos et al. (2001)
57	25–32	60–66	~34	18.6	Sartori et al. (2003)
64	26–58	Term	~238	8.6	Szenci et al. (1998)
148	28	98	70	18.9	Vasconcelos et al. (1999)
Overall: 6195	25–70	56–term	28–250	10.7 (8.3–24.0)	
Primigravid					
72	30	Term	~250	4.2	Dunne et al. (2000)
1933	35–48	Term	~238	1.5	Ettema and Santos (in press)
1050	41	120–150	84	2.8	Labèrnia et al. (1996)
147	30	75	45	10.2	Rivera et al. (in press)
131	28	84	56	6.05	Silke et al. (2002)
Overall: 3333	28–58	75–term	45–250	2.52 (1.5–10.2)	



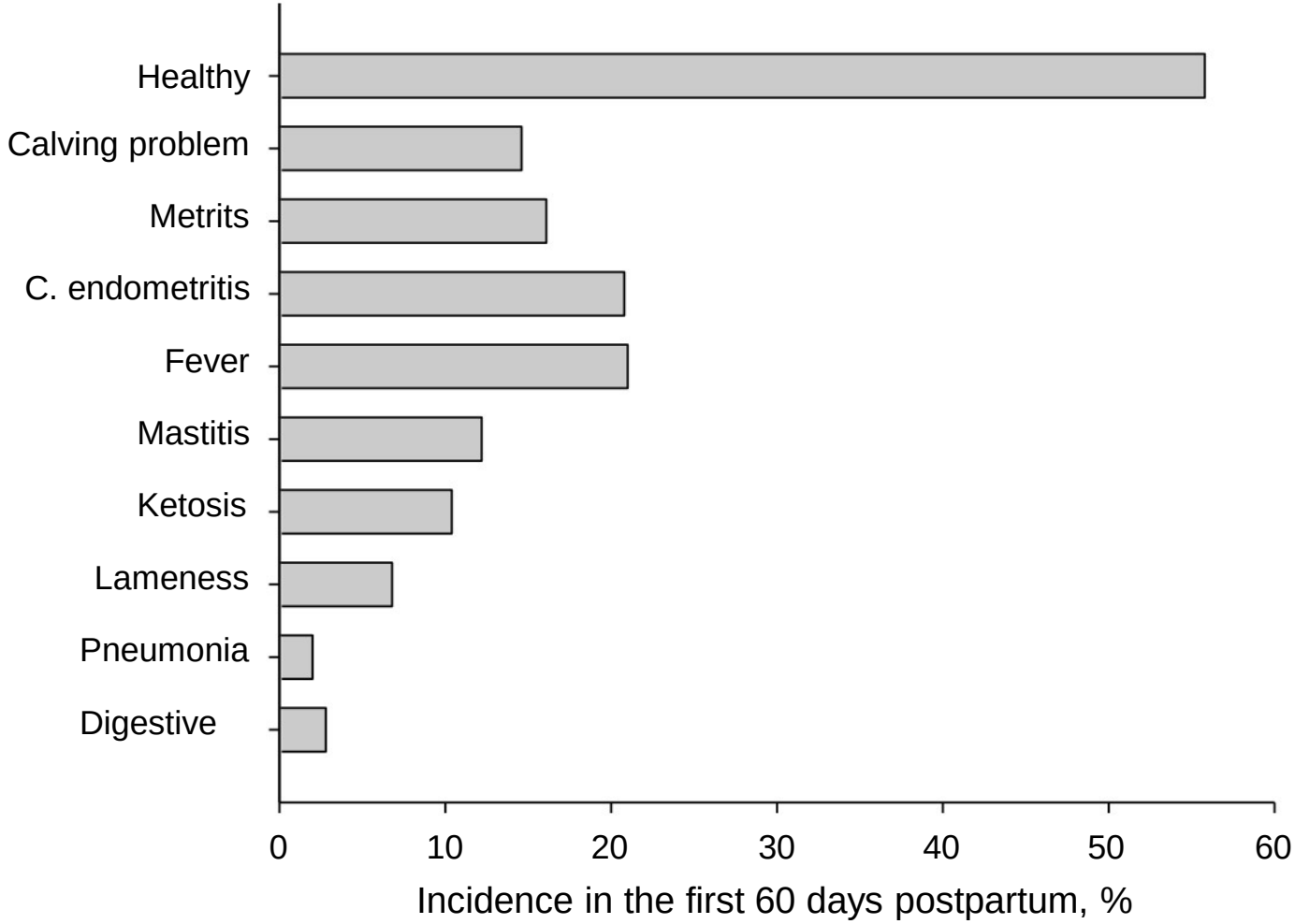
Adapted from Santos *et al.,* 2004; ARS

Summary

- **Lactating dairy cows**
  - Fertilization rate = ~ 76% (55% heat stress, ~ 80% cool weather)
  - Viable embryos = ~50% of oocytes (18% heat stress, ~60% cool weather)
  - Late embryonic loss = ~13% (43% heat stress)
  - Fetal losses = ~ 10%
  - Greatest risk in the first 42 d of gestation (0.9%/d)
    - ☐With early pregnancy diagnosis (~30 d), confirmation is critical
- **Heifers**
  - Fertilization rate ≥ 90%
  - Late embryonic and fetal mortality < 5.0%

Incidence of infectious diseases in the first 60 d postpartum

- **5,719 cows from 7 dairies in the US**



(Santos et al., 2010. Soc Reprod Fertil Suppl.)

Disease and Pregnancy 35d

Health status	CR, %	Adjusted OR (95% CI)	*P*
Healthy	51.4	1.00	
1 case of disease	43.3	0.79 (0.69 - 0.91)	0.001
> 1 case of disease	34.7	0.57 (0.48 - 0.69)	< 0.001
Type of health problem			
Calving problem	40.3	0.75 (0.63 - 0.88)	< 0.001
Metritis	37.8	0.66 (0.56 - 0.78)	< 0.001
Clinical endometritis	38.7	0.62 (0.52 - 0.74)	< 0.001
Fever postpartum	39.8	0.60 (0.48 - 0.65)	< 0.001
Mastitis	39.4	0.84 (0.64 - 1.10)	0.20
Clinical ketosis	28.8	0.50 (0.36 - 0.68)	< 0.001
Lameness	33.3	0.57 (0.41 - 0.78)	< 0.001
Pneumonia	32.4	0.63 (0.32 - 1.27)	0.20
Digestive problem	36.7	0.78 (0.46 - 1.34)	0.38

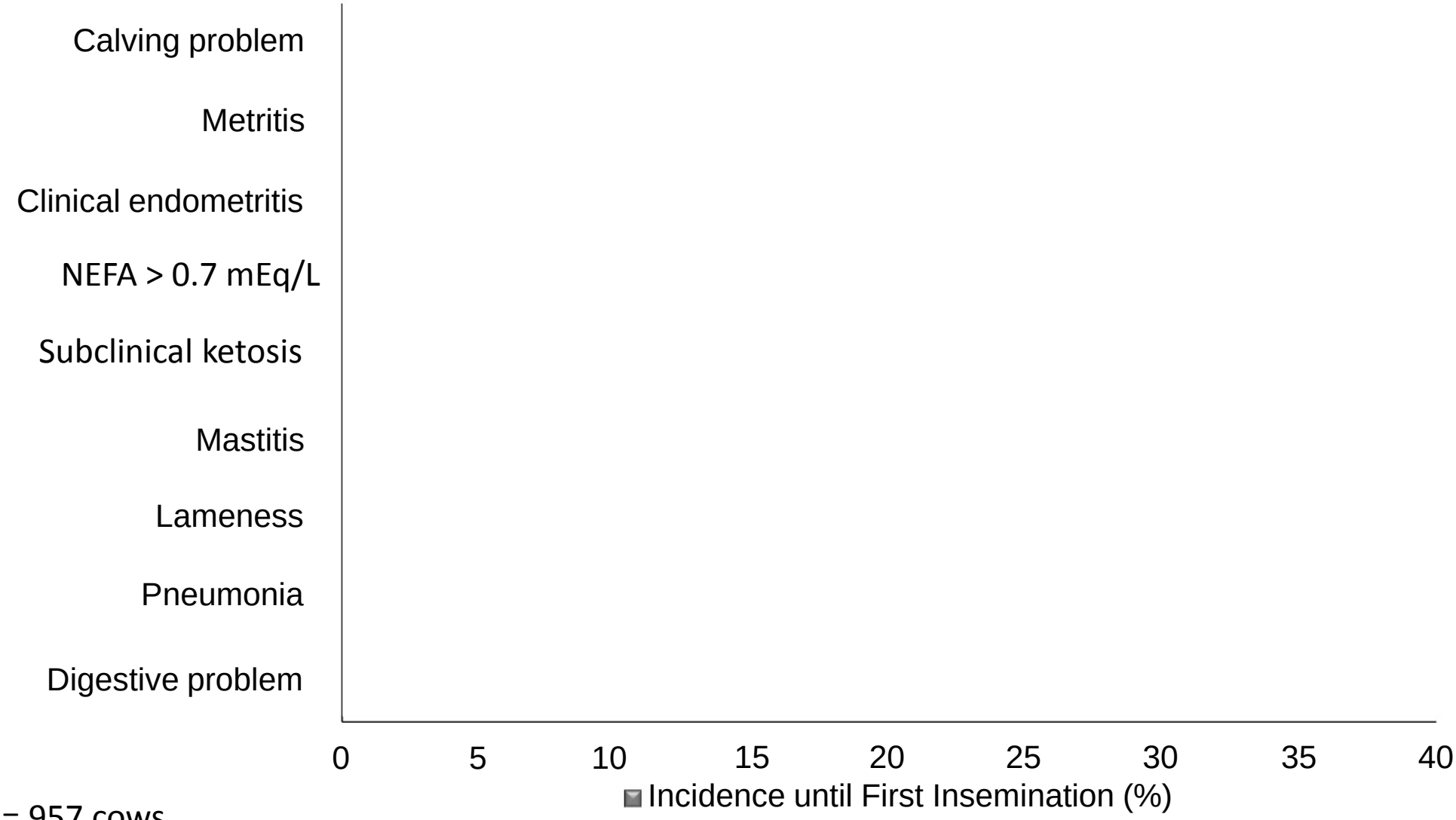
(Santos et al., 2010. Soc Reprod Fertil Suppl.)

Disease and Pregnancy Loss 35-70d

Health status	Loss, %	Adjusted OR (95% CI)	*P*
Healthy	8.9	1.00	---
1 case of disease	13.9	1.73 (1.25 - 2.39)	< 0.001
> 1 case of disease	15.8	2.08 (1.36 - 3.17)	< 0.001
Type of health problem			
Calving problem	15.9	1.67 (1.16 - 2.40)	< 0.01
Metritis	11.3	1.01 (0.71 - 1.60)	0.76
Clinical endometritis	15.1	1.55 (1.04 - 2.32)	0.03
Fever postpartum	18.0	2.00 (1.24 - 3.14)	< 0.01
Mastitis	19.8	2.62 (1.48 - 4.64)	< 0.001
Clinical ketosis	14.6	1.64 (0.75 - 3.59)	0.22
Lameness	26.4	2.67 (1.38 - 5.12)	< 0.01
Pneumonia	16.7	1.87 (0.40 - 8.69)	0.42
Digestive problem	15.8	1.81 (0.52 - 6.32)	0.35

(Santos et al., 2010. Soc Reprod Fertil Suppl.)

Incidence of infectious diseases in the first 60 d postpartum



N = 957 cows

Ribeiro et al., 2013; JDS

Disease and Pregnancy 30d

Category	Pregnant, %	Adjusted OR (95% CI)	*P*
Healthy	70.9	1.00	---
1 case of disease	61.4	0.67 (0.47 - 0.94)	0.02
> 1 case of disease	48.5	0.42 (0.29 - 0.60)	< 0.01
Type of health problem			
Calving problem	44.8	0.51 (0.29 - 0.91)	0.02
Metritis	38.6	0.36 (0.19 - 0.67)	< 0.01
Clinical endometritis	54.1	0.72 (0.48 - 1.07)	0.10
NEFA > 0.7 mEq/L	45.6	0.47 (0.32 - 0.70)	< 0.01
Subclinical ketosis	56.8	0.70 (0.51 - 0.96)	0.03
Mastitis	54.4	0.66 (0.45 - 0.98)	0.04
Lameness	45.8	0.52 (0.23 - 1.17)	0.11
Pneumonia	45.0	0.59 (0.24 - 1.45)	0.25
Digestive problem	32.0	0.30 (0.13 - 0.70)	<0.01

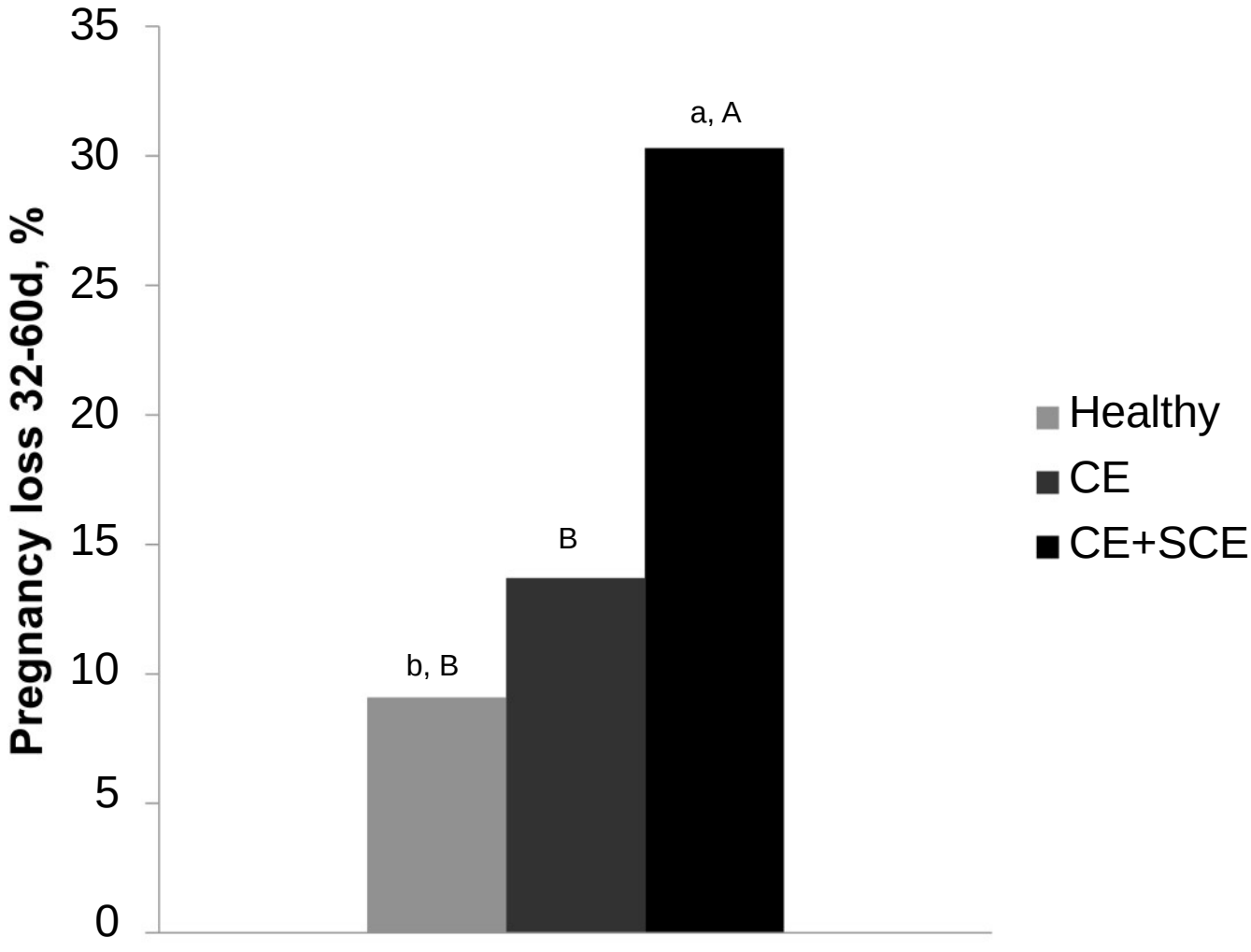
Ribeiro et al., 2013; JDS

Disease and Pregnancy Loss 30-65d

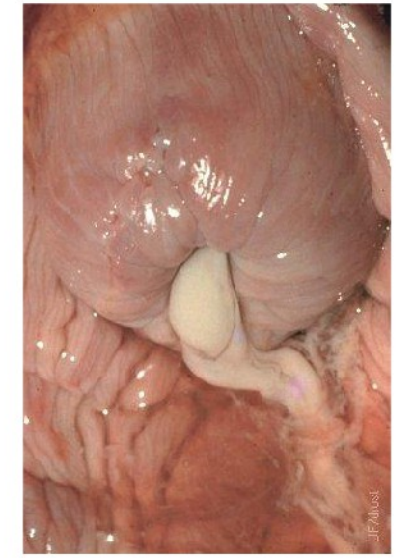
Health status	Loss, %	Adjusted OR (95% CI)	*P*
Healthy	10.4	1.00	---
1 case of disease	9.0	0.91 (0.46 - 1.82)	0.80
> 1 case of disease	15.0	1.71 (0.86 - 3.39)	0.13
Type of health problem			
Calving problem	26.9	3.89 (1.53 - 9.93)	< 0.01
Metritis	31.2	4.06 (1.34 - 12.29)	0.01
Clinical endometritis	20.6	2.55 (1.28 - 5.07)	< 0.01
NEFA > 0.7 mEq/L	6.6	0.67 (0.23 - 1.99)	0.48
Subclinical ketosis	8.3	0.92 (0.44 - 1.92)	0.82
Mastitis	12.3	1.02 (0.45 - 2.31)	0.96
Lameness	0.0	---	---
Pneumonia	22.2	2.93 (0.58 - 14.90)	0.20
Digestive problem	12.5	1.28 (0.15 - 10.72)	0.82

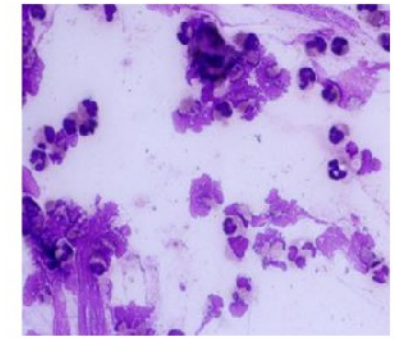
Ribeiro et al., 2013; JDS

Endometritis and Pregnancy Loss

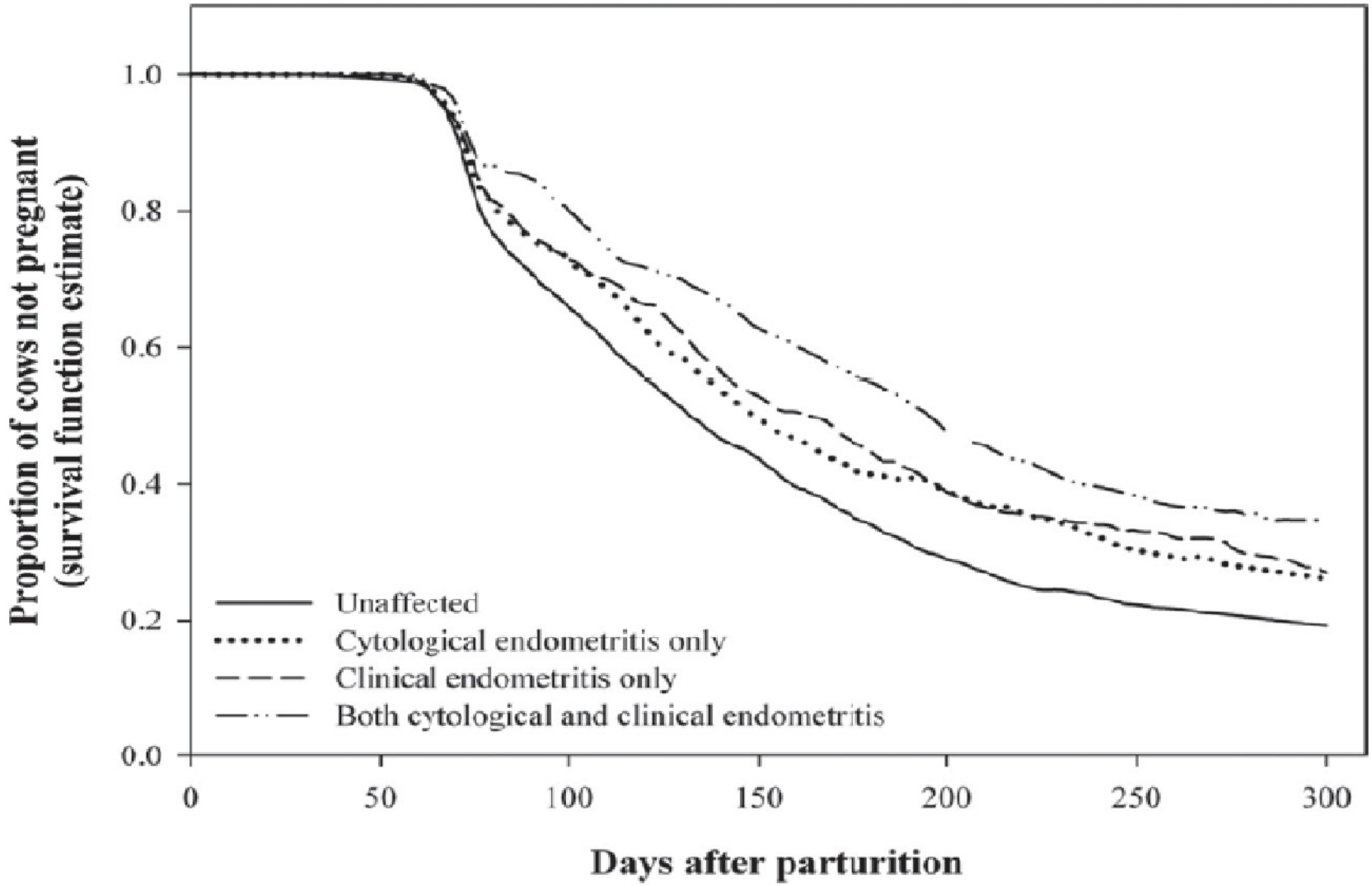


Lima et al., 2013; JDS





Time to Pregnancy



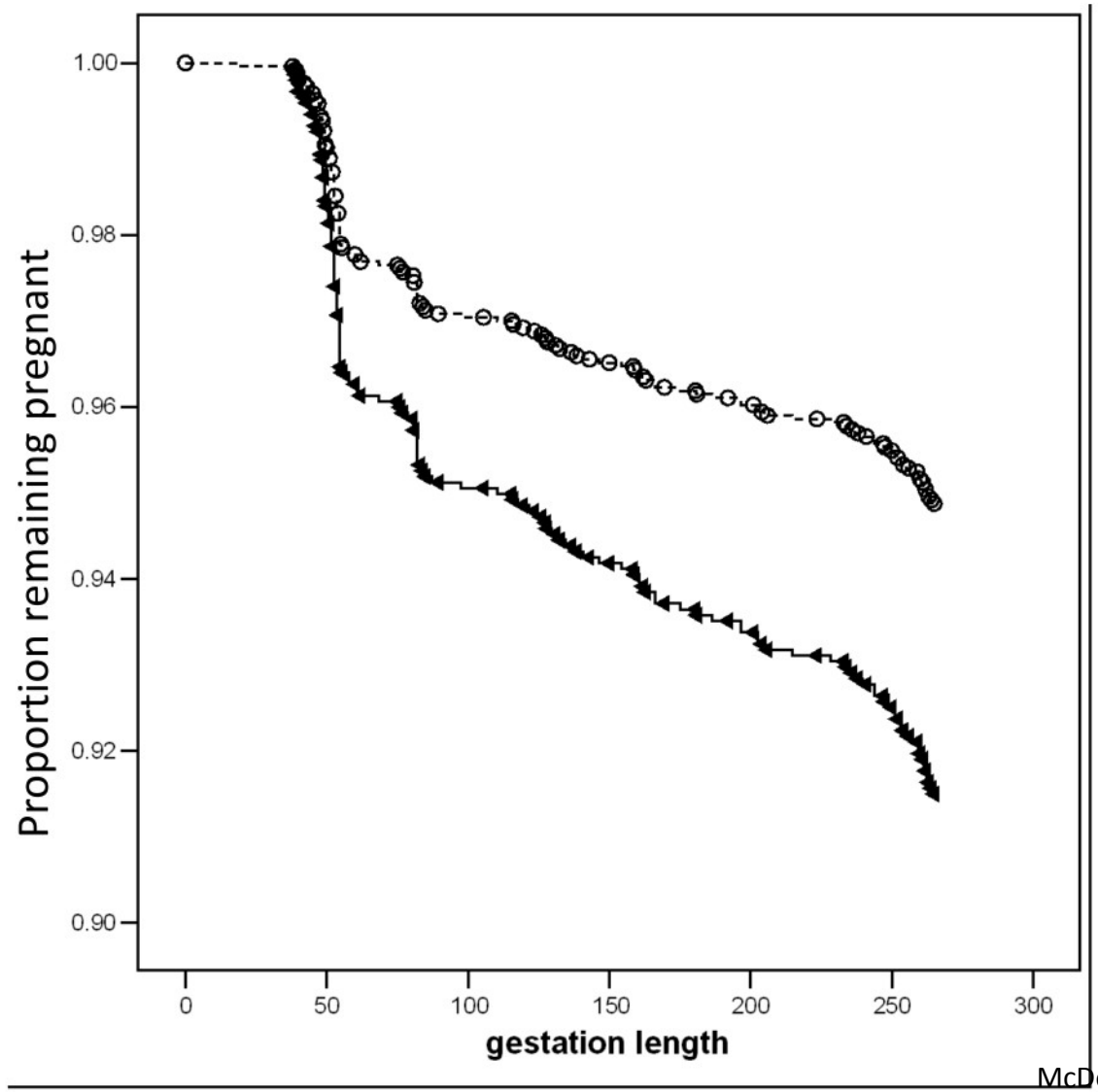
Dubuc et al., 2011; JDS

Effect of Cyclicity Status Prior to Insemination on Late Embryonic Losses in Dairy Cows, % (No. Pregnancies)

Reference	Status		*P* =
	Cyclic	Anovular	
Bisinotto *et al.* (2010)	13.2 (1,780)	15.0 (374)	0.17
Cartmill *et al.* (2001)	24.0 (223)	33.0 (33)	NS
Cartmill *et al.* (2001)	36.8 (95)	80.0 (15)	0.05
Cerri *et al.* (2003)	10.8 (204)	14.6 (48)	NS
Chebel *et al.* (2010)	8.7 (207)	13.3 (60)	0.30
Gumen *et al.* (2003)	12.3 (81)	20.0 (5)	NS
McDougall *et al.* (2005)	5.0 (1,470)	9.0 (534)	0.007
Pursley *et al.* (2001)	15.1 (186)	35.0 (46)	---
Santos *et al.* (2004)	10.4 (270)	17.5 (40)	NS
Santos *et al.* (2004)	10.2 (186)	7.7 (26)	NS
Stevenson *et al.* (2006)	16.0 (208)	31.0 (81)	< 0.05

Anovular vs. Cyclic: Relative Risk = 1.35 (95% CI = 1.16-1.58)

Proportion of Cows Classified as Cyclic (o) and Anestrus (▲) Remaining Pregnant



N = 2,004 cows
10 dairy herds

McDougall *et al. N. Zeal. Vet. J. (2005)*

What Factors Affect Cyclicity?

Table 3. Final multivariable logistic regression model (model 1) for factors associated with cyclicity by 21 ± 3 DIM including all cows (n = 768)

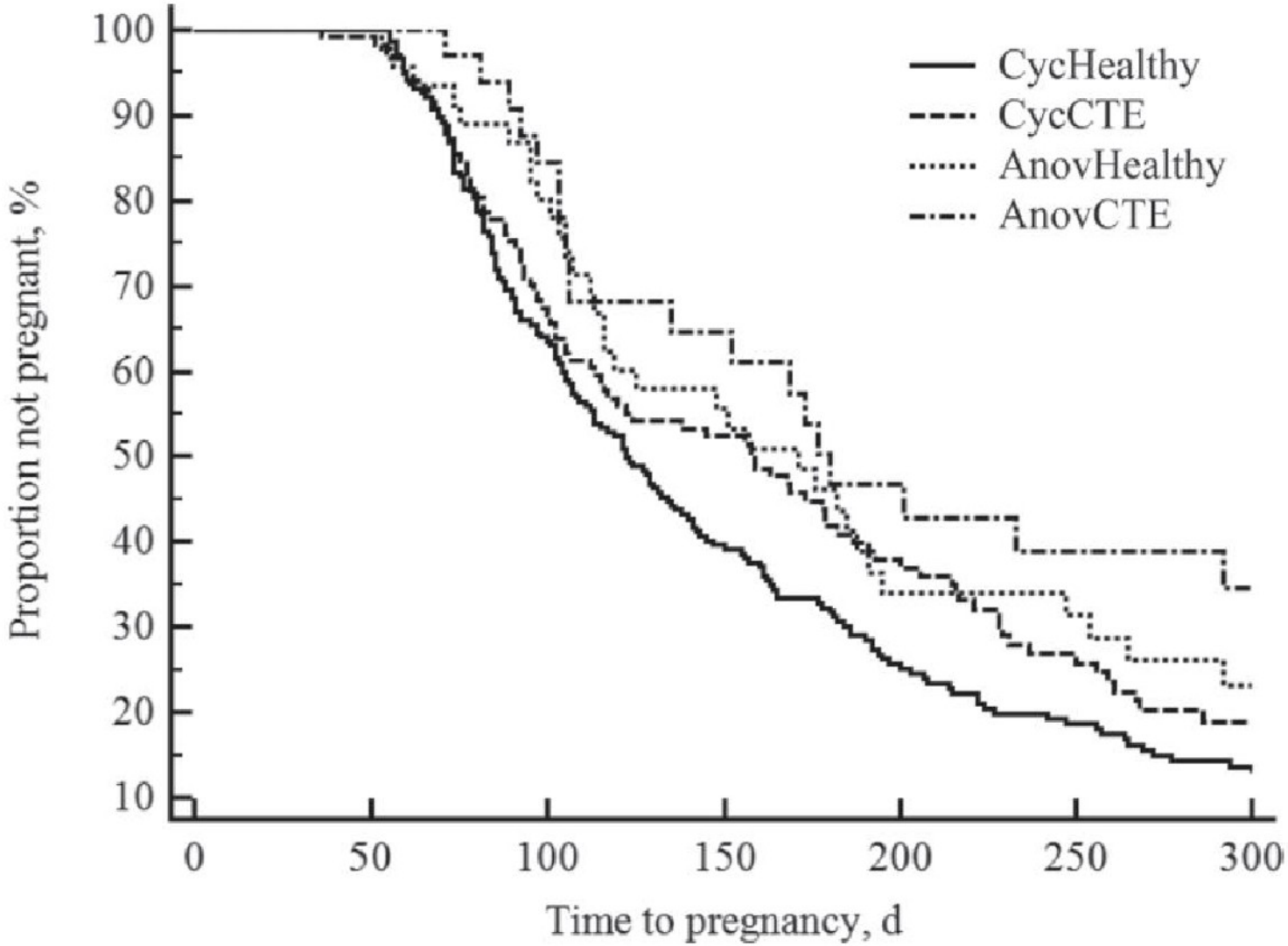
Variable	Level	Cows, no.	Cyc21,[1] %	Odds ratio	95% CI	*P*-value
Calving season[2]	SumFall	598	45.7	2.4	1.6–3.6	<0.001
	WinSpri	170	27.7	Ref.[3]	Ref.	—
Parity	Multiparous	445	45.4	1.5	1.1–2.1	0.01
	Primiparous	323	36.5	Ref.	Ref.	—
Metabolic problem[4]	No	599	43.7	1.7	1.2–2.6	0.005
	Yes	169	34.3	Ref.	Ref.	—
Digestive problem[5]	No	696	42.8	1.8	1.0–3.1	0.05
	Yes	72	30.6	Ref.	Ref.	—

Table 4. Final multivariable logistic regression model (model 2) for factors associated with cyclicity by 21 ± 3 DIM including cows that had BW measured (only dairy 1; n = 458)

Variable	Level	Cows, no.	Cyc21,[1] %	Odds ratio	95% CI	*P*-value
Calving season[2]	SumFall	300	50.0	2.7	1.7–4.1	<0.001
	WinSpri	158	28.5	Ref.[3]	Ref.	—
Metritis[4]	No	344	46.2	1.7	1.1–2.8	0.02
	Yes	114	31.6	Ref.	Ref.	—
Digestive problem[5]	No	387	45.0	1.9	1.1–3.3	0.03
	Yes	71	29.6	Ref.	Ref.	—
BWL[6]	≤28 kg	157	49.0	1.5	1.0–2.3	0.06
	>28 kg	301	39.2	Ref.	Ref.	—

Vercouteren et al., 2014; JDS

Combined effect of Anovulation and CTE



Vieira-Neto et al., 2014; JDS

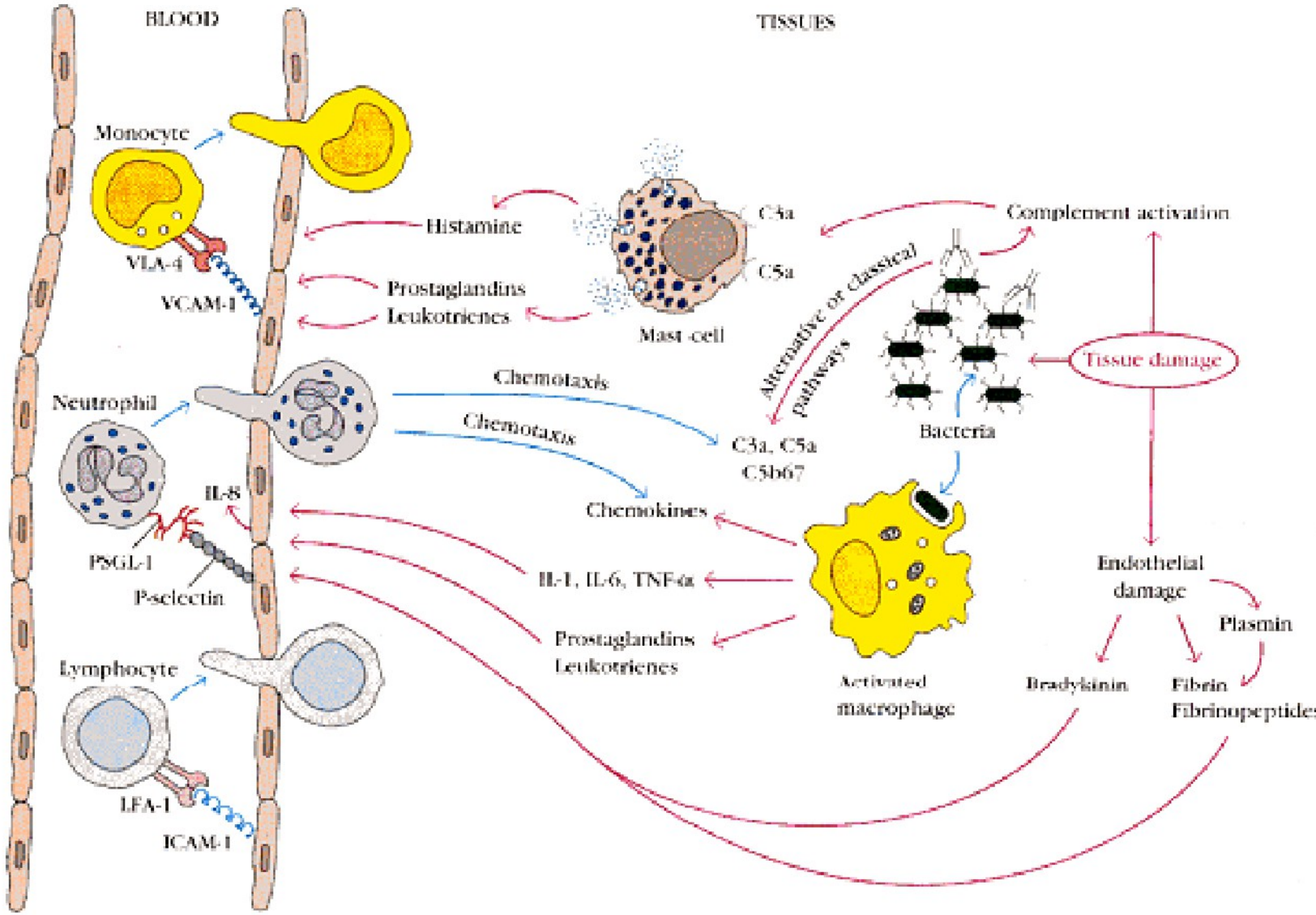
Summary

- There is no good disease!!!

What leads to disease?

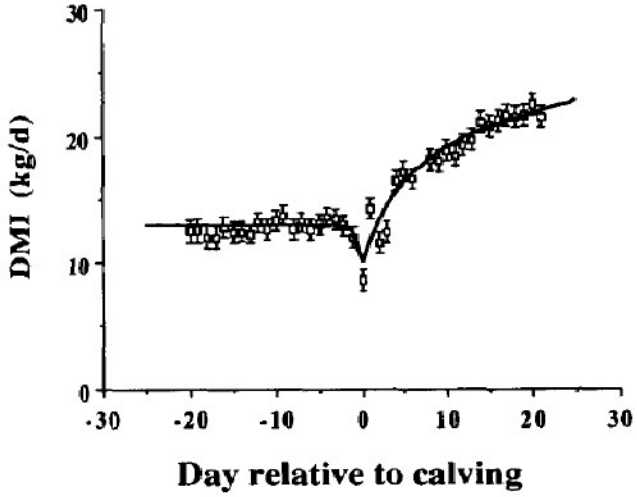
- Disease is multifactorial

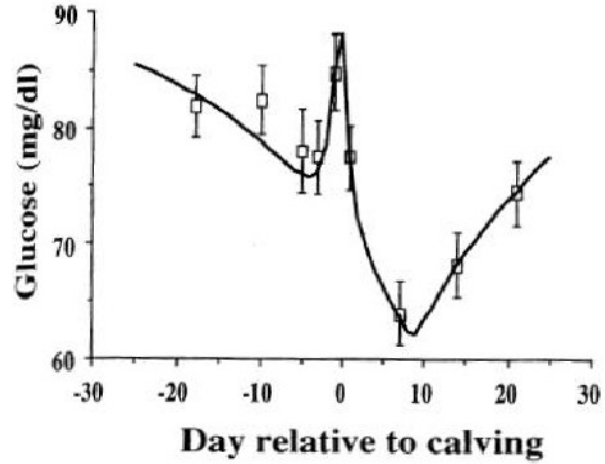
Infection and the Immune System

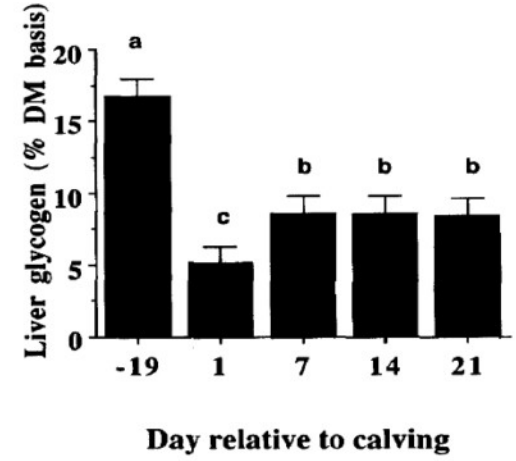


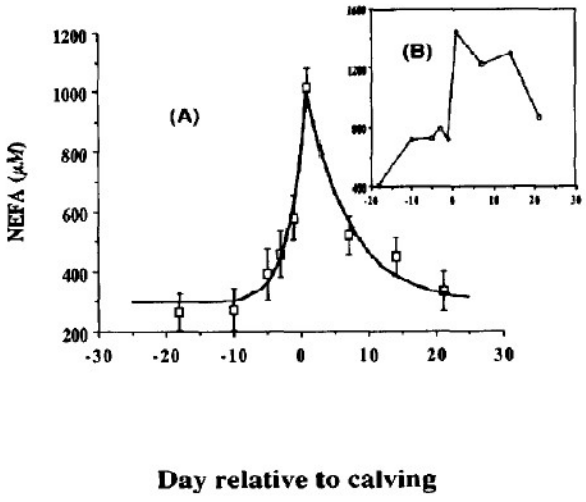
Kuby Immunology, 6th ed.

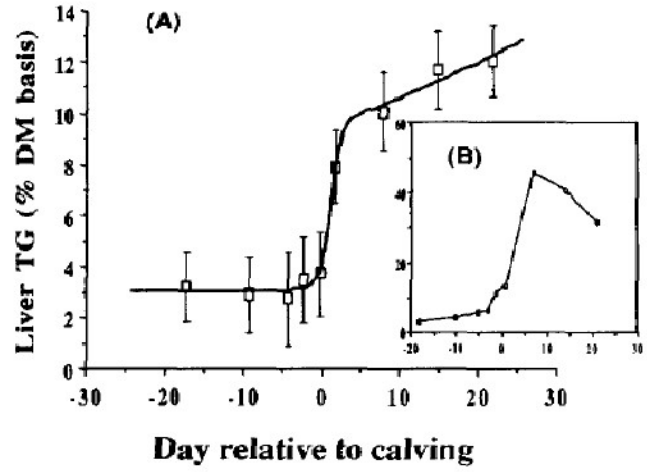
Metabolic State Peripartum

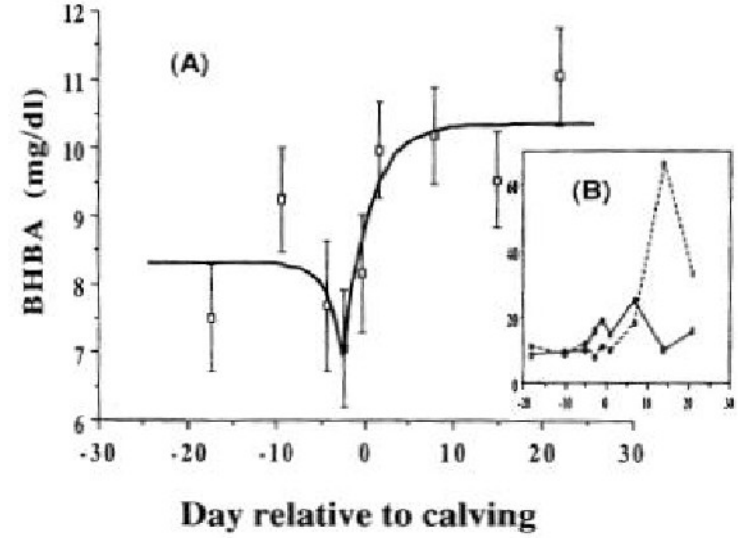






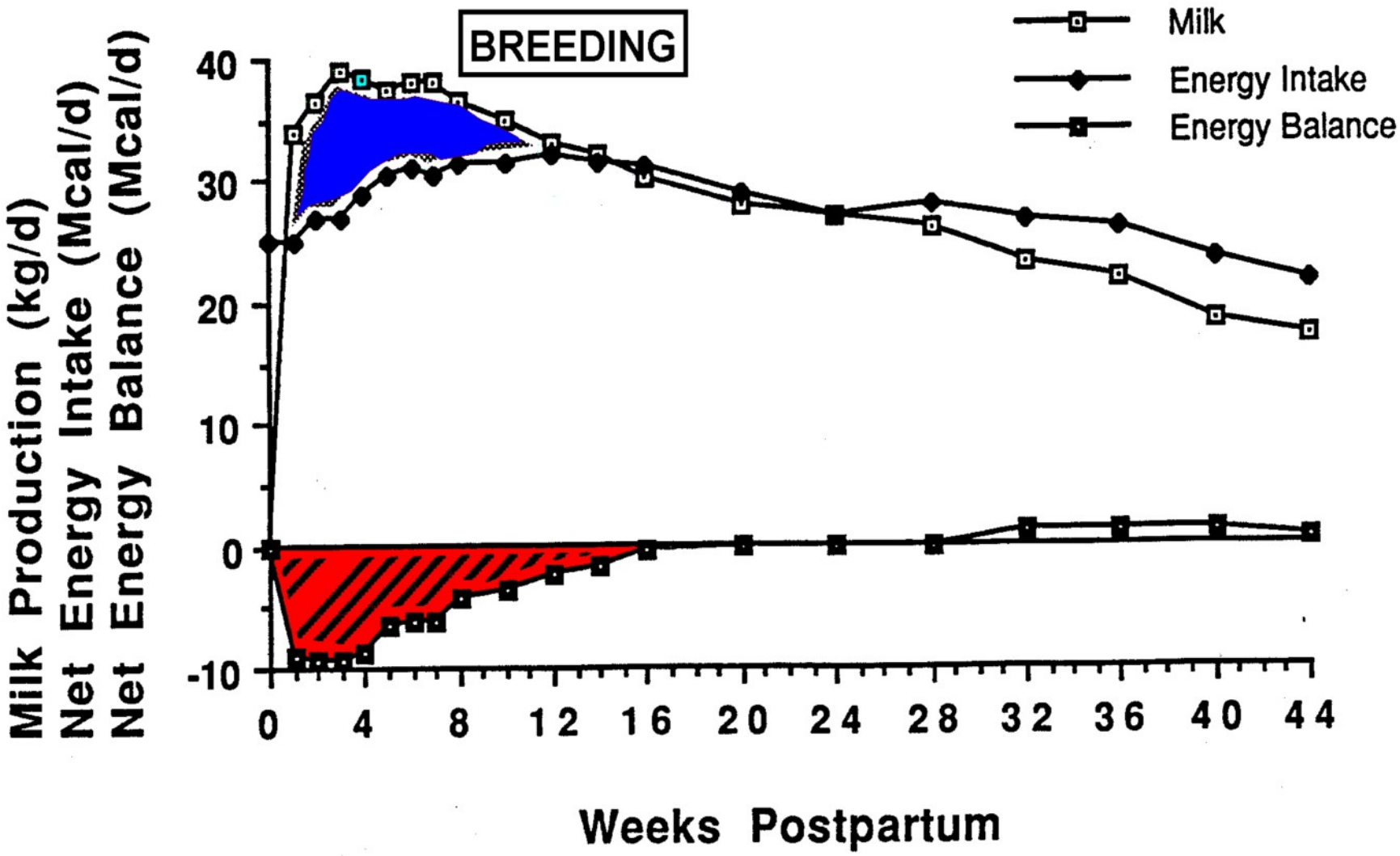






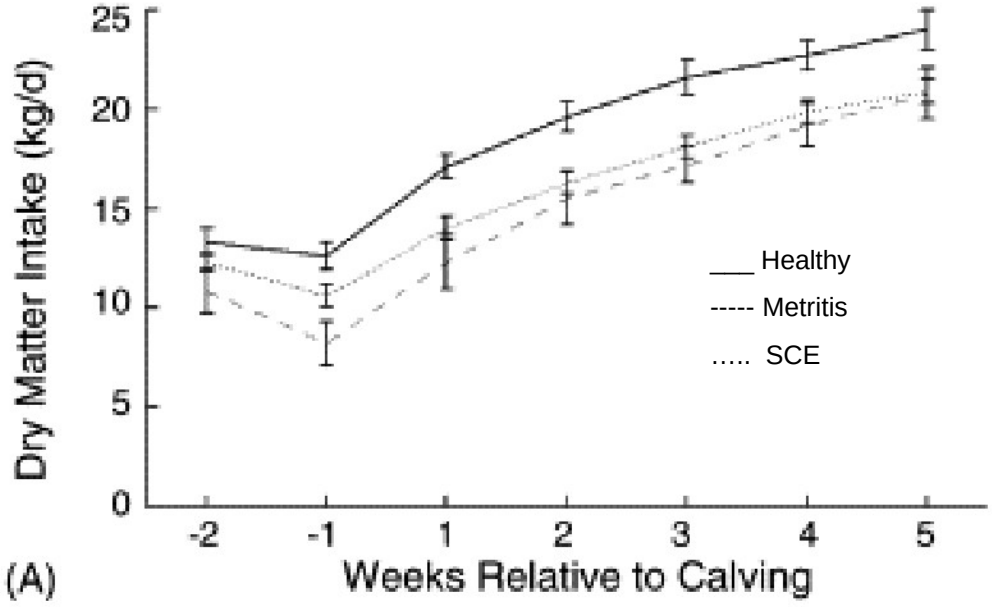
Vazquez-Añon et al., 1994; JDS

NEB in Early Lactation

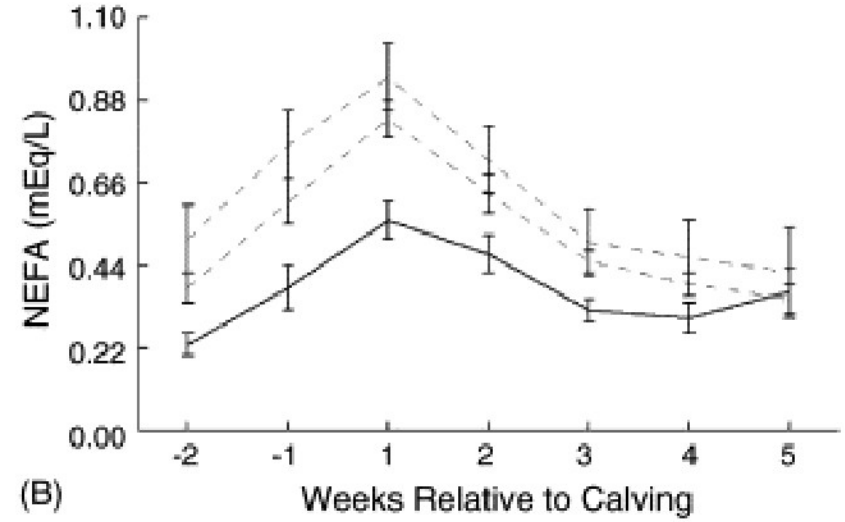


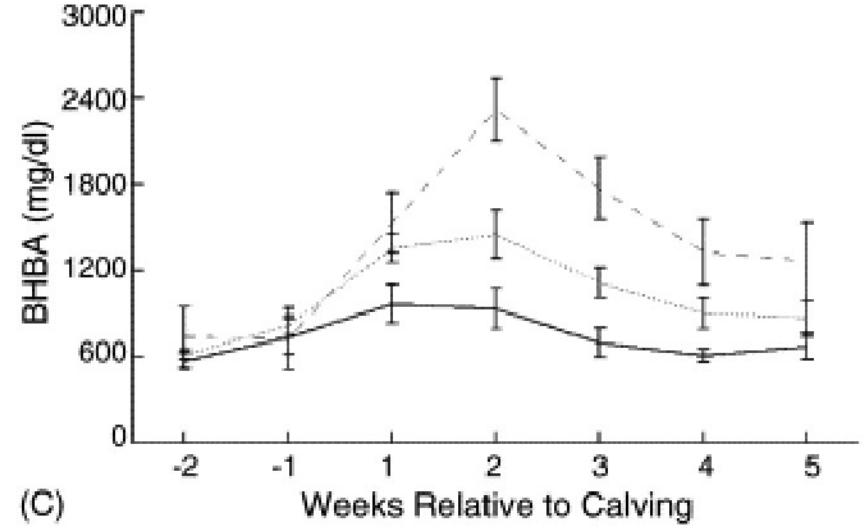
Courtesy of Dr. WR Butler

DMI and Uterine Disease

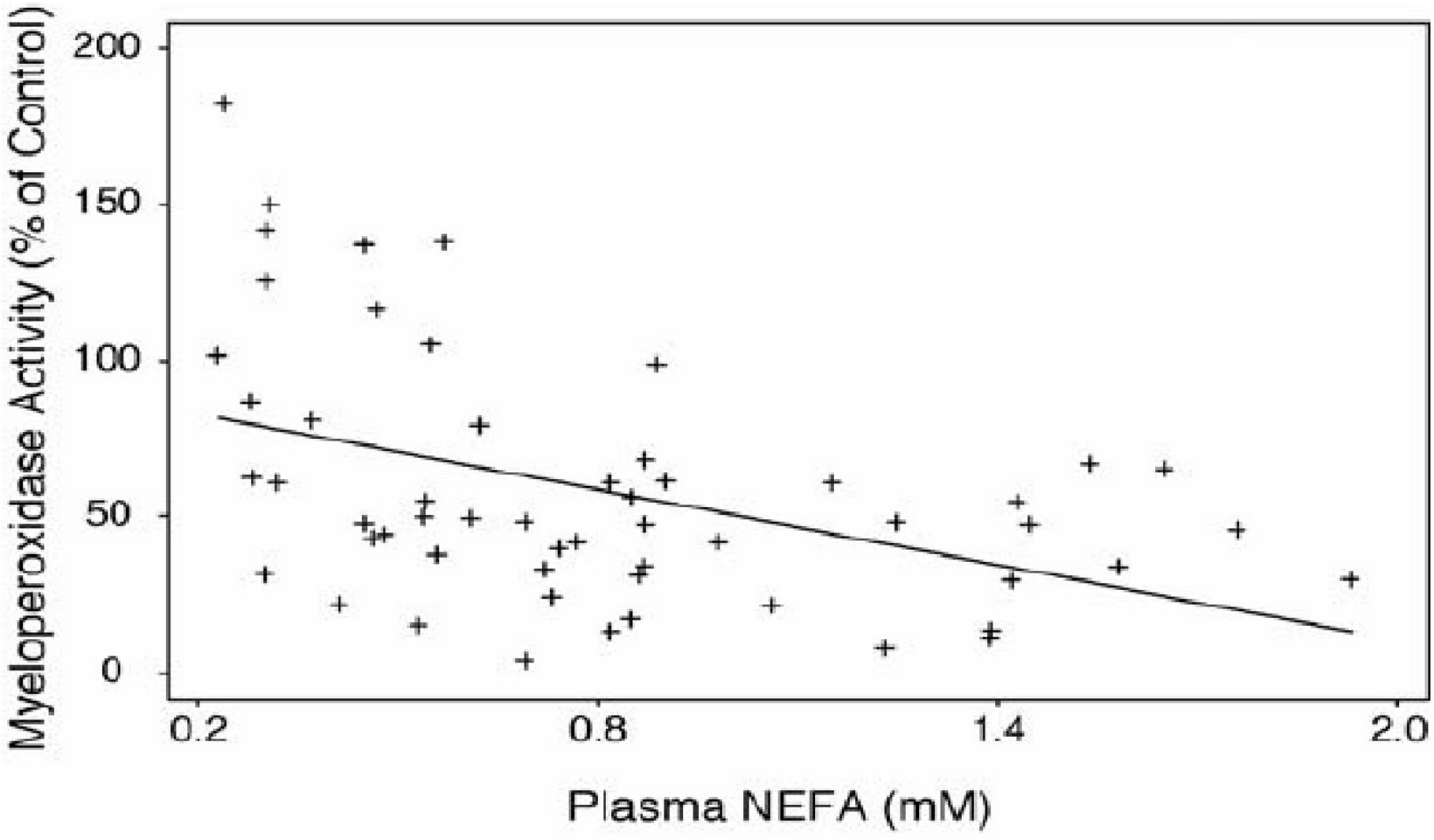


Hammon et al., 2006; Vet. Imm. Immunop.



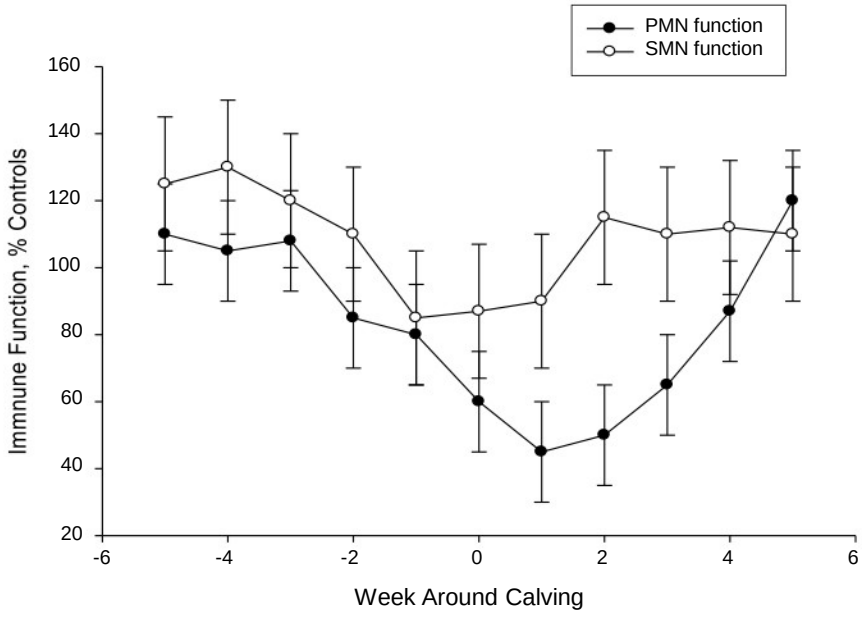


NEFA and Immune Function

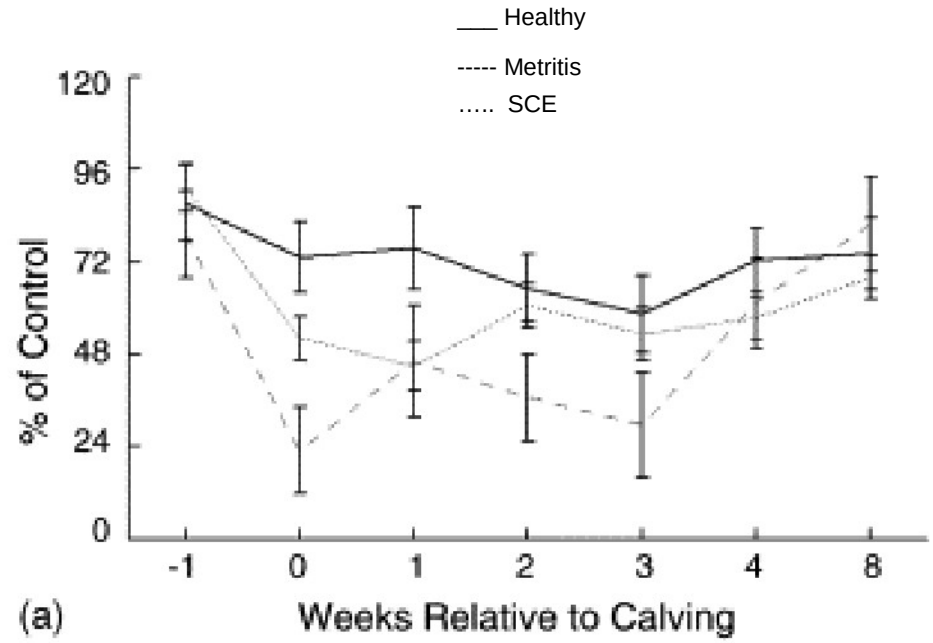


Hammon et al., 2006; Vet. Imm. Immunopath.

Immunosuppression

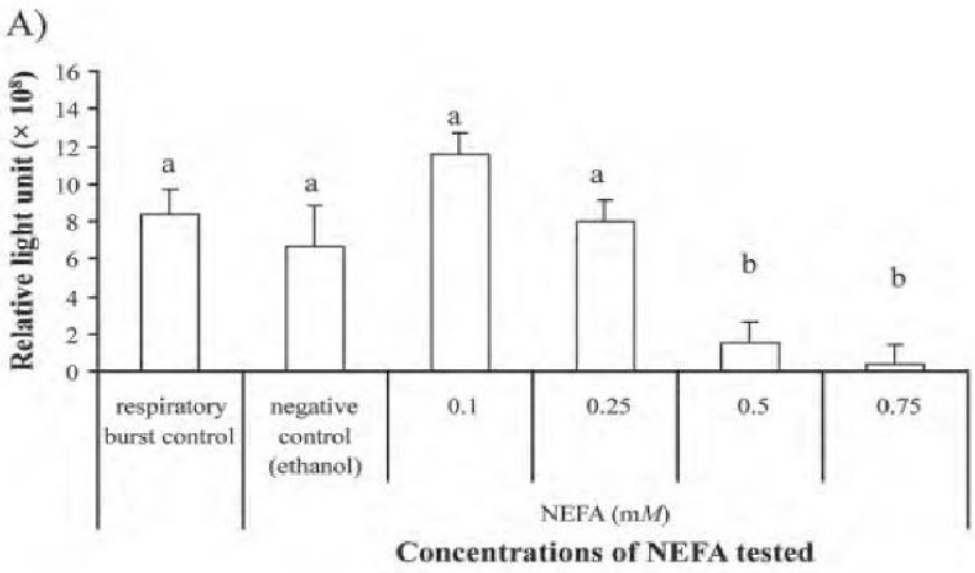


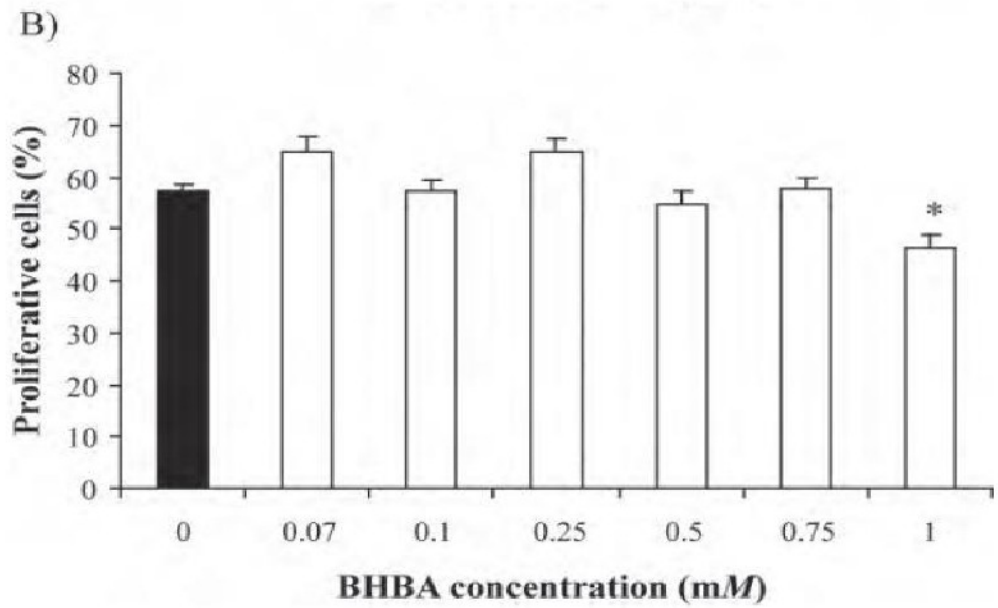
Kehrli et al., 1989; JDS



Hammon et al., 2006; Vet Im Im

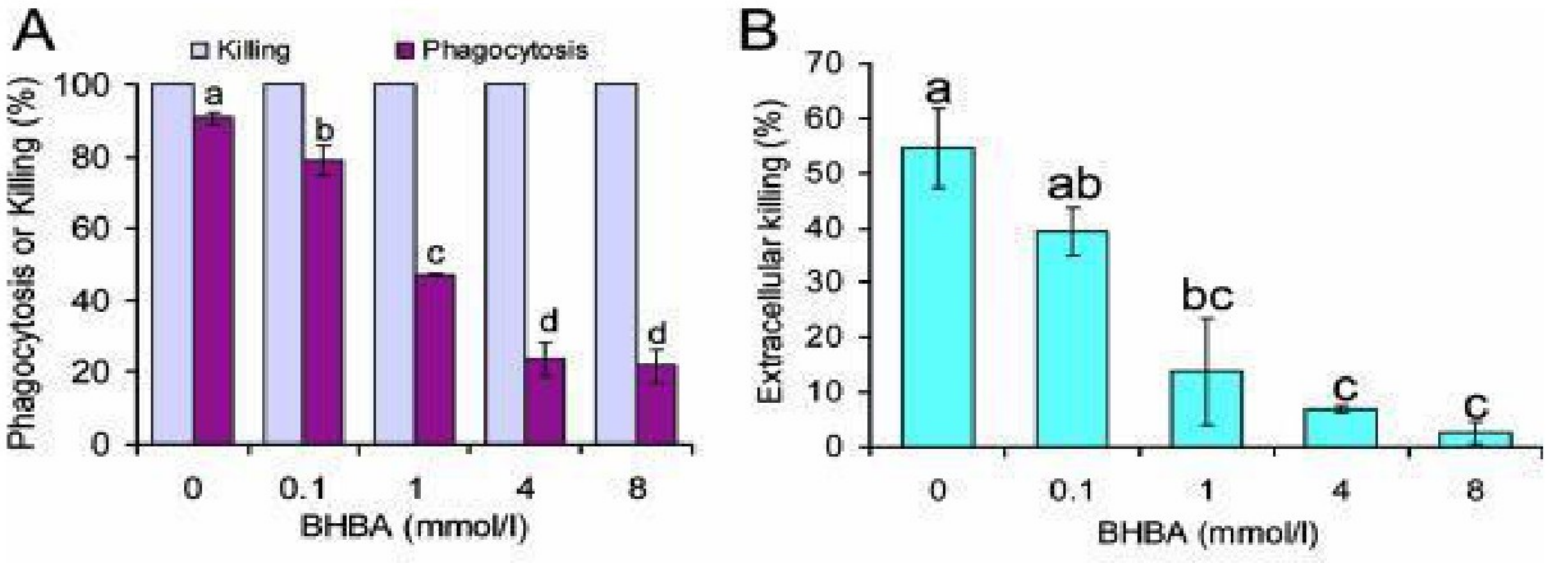
NEFA & BHBA & Immune Function



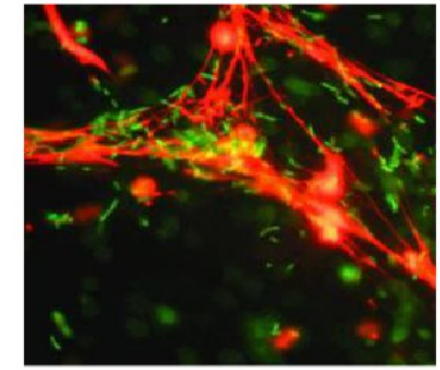


Ster et al., 2012; JDS

BHBA and Immune Function

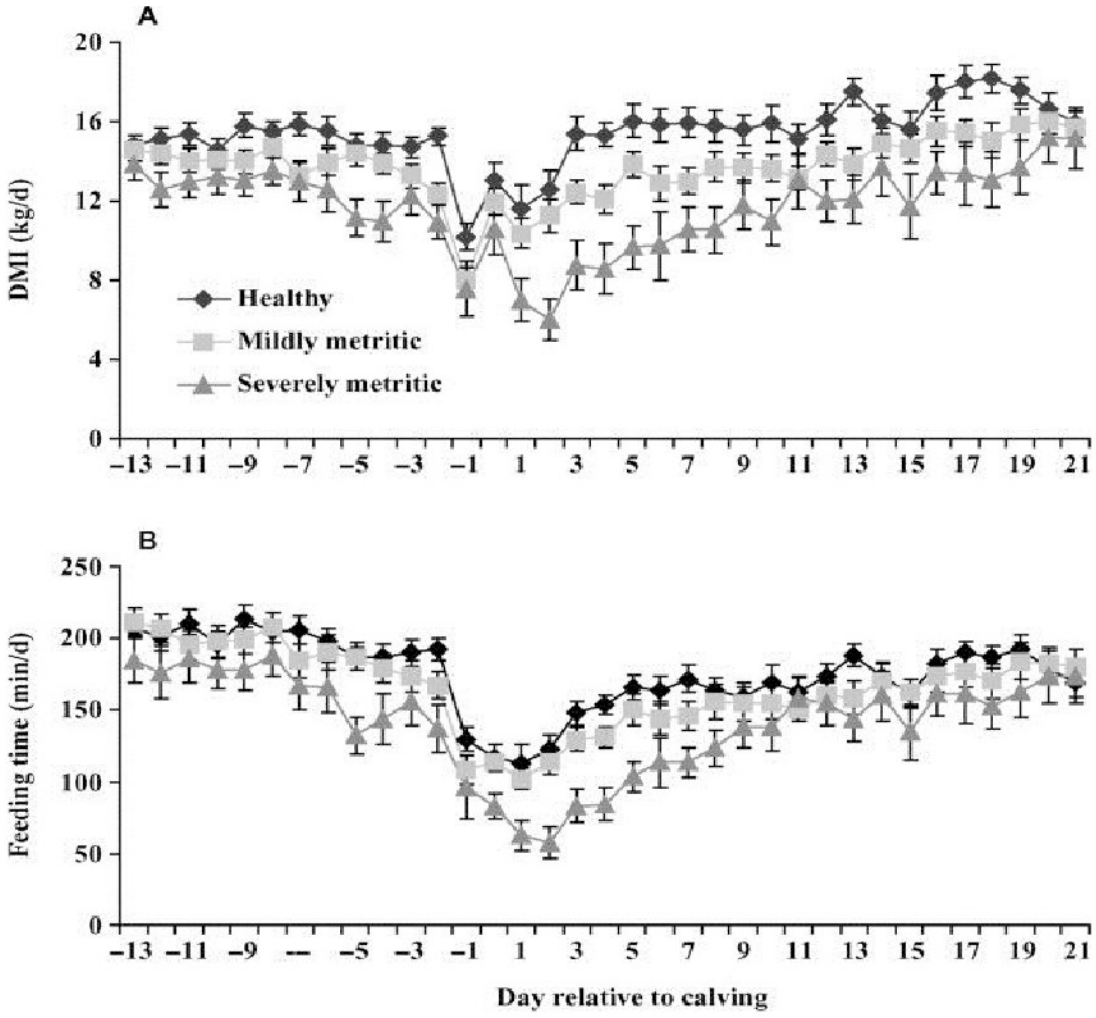


Grinberg et al., 2008; Infec. Immun.



Papayannopoulos et al. 2010. J. Cell Biol.

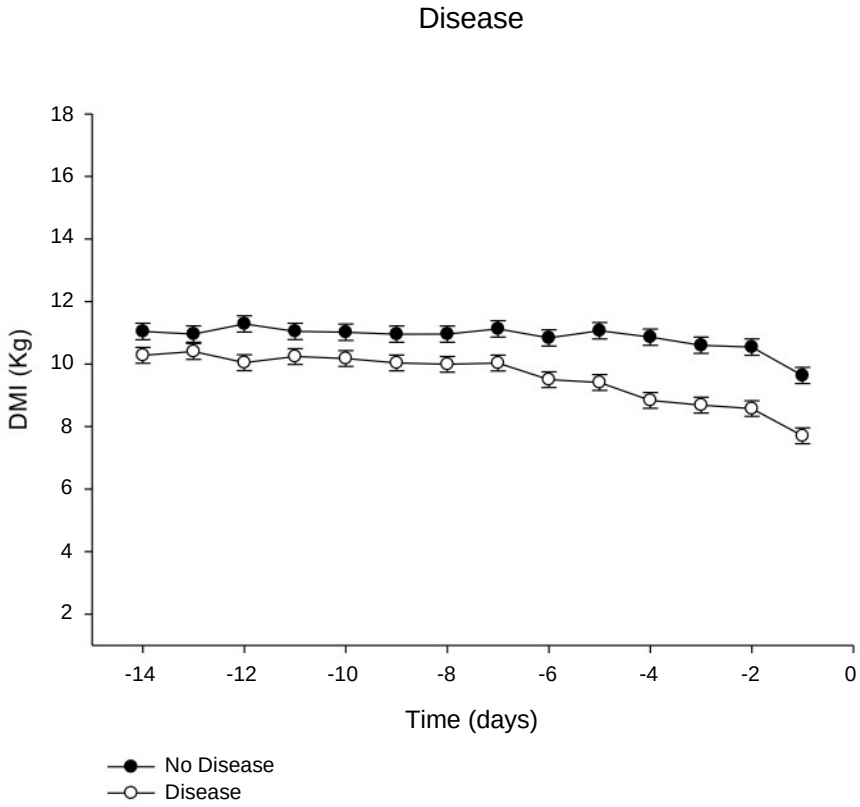
DMI and Uterine Disease

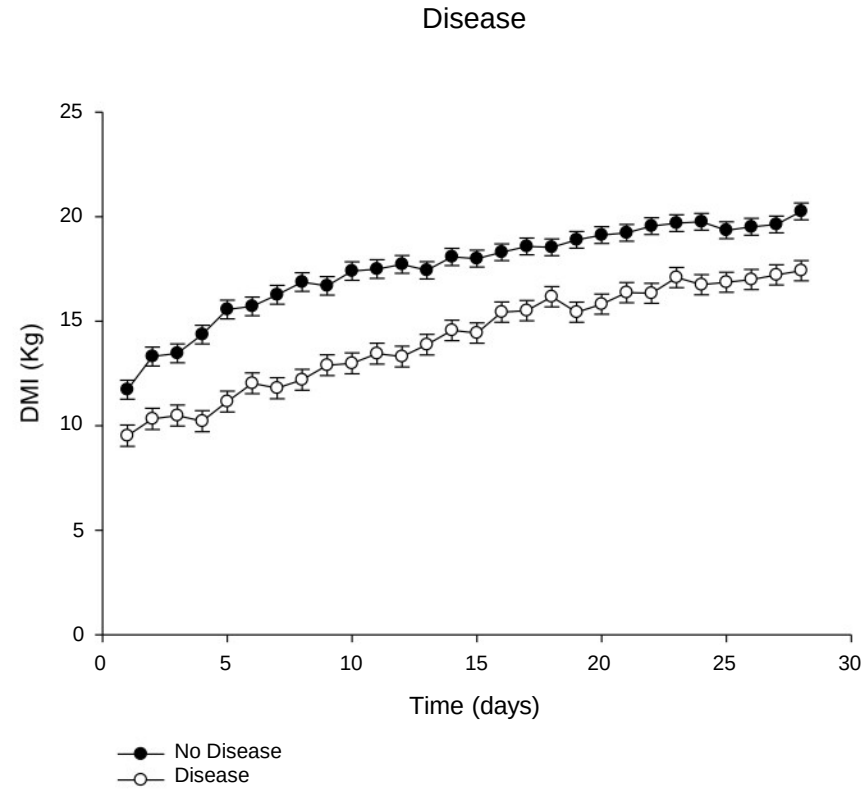


Huzzey et al., 2007; JDS

- Each kg decrease in DMI the last week prepartum increased the odds of severe metritis by 187% (OR = 2.87; P = 0.02)
- Each 10 min decrease in feeding time during the last week prepartum increased the odds of severe metritis by 72% (OR = 1.72; P = 0.02)

DMI Pre- and Postpartum





- Disease = RP, metritis, mastitis, ketosis or DA (n = 167; 57%)
- Each kg decrease in DMI the last week prepartum increased the odds of postpartum disease by 18% (OR = 1.18; P < 0.01)

Perez et al., 2014; unpublished

Calcium during transition

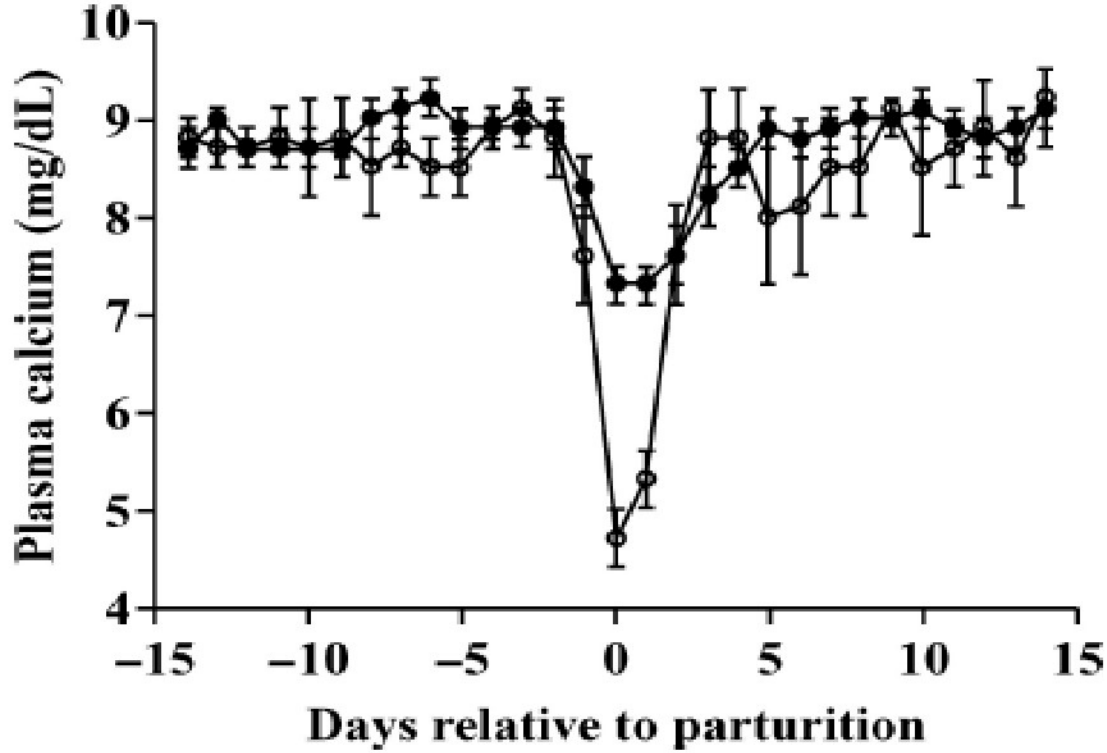
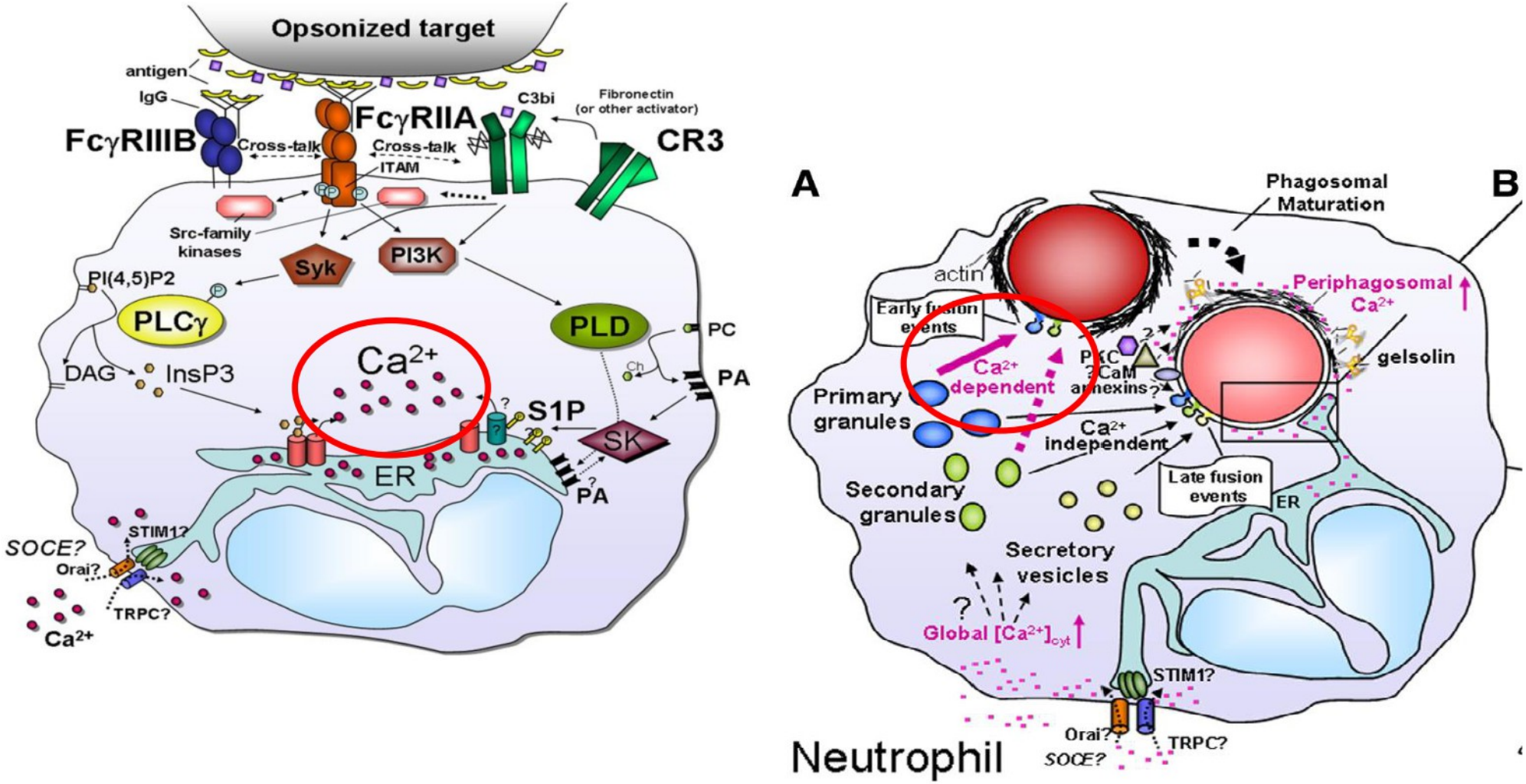


Figure 1. Plasma calcium concentrations (mean ± SEM) around the time of parturition in milk fever (○; n = 8) and nonmilk fever (●; n = 19) cows; d 0 = day of parturition.

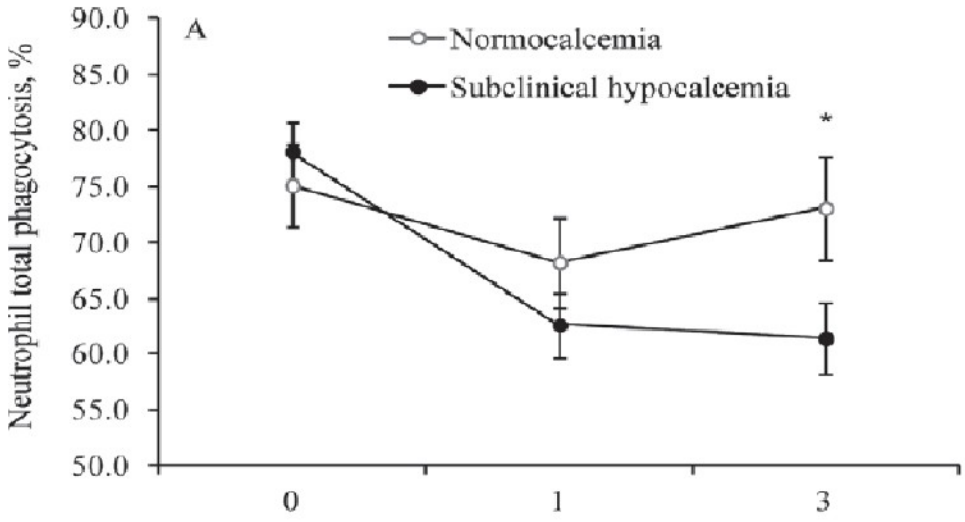
Kimura et al., 2006; JDS

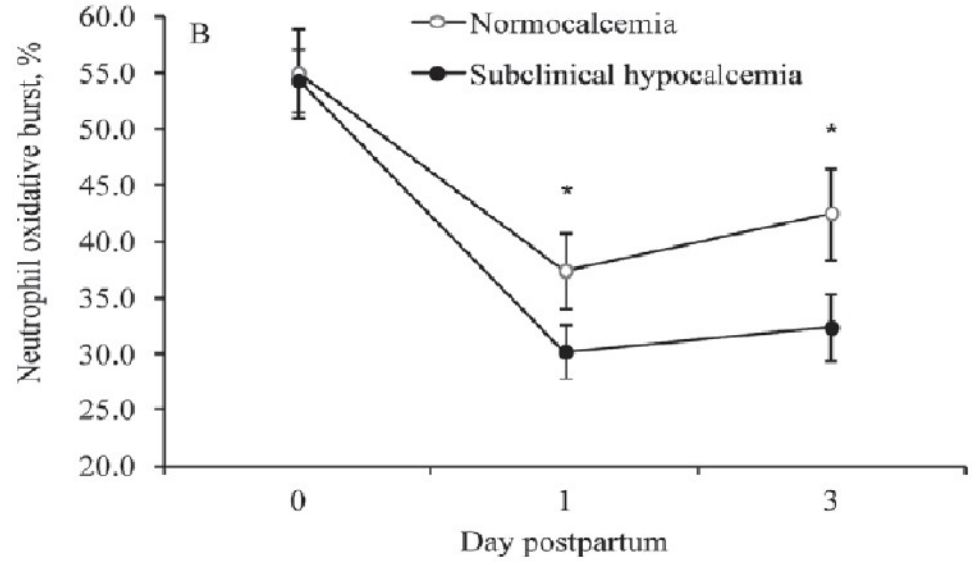
Calcium Activates Leukocytes



Nunez and Demaurex, Journal of Leukocyte Biology, 2010

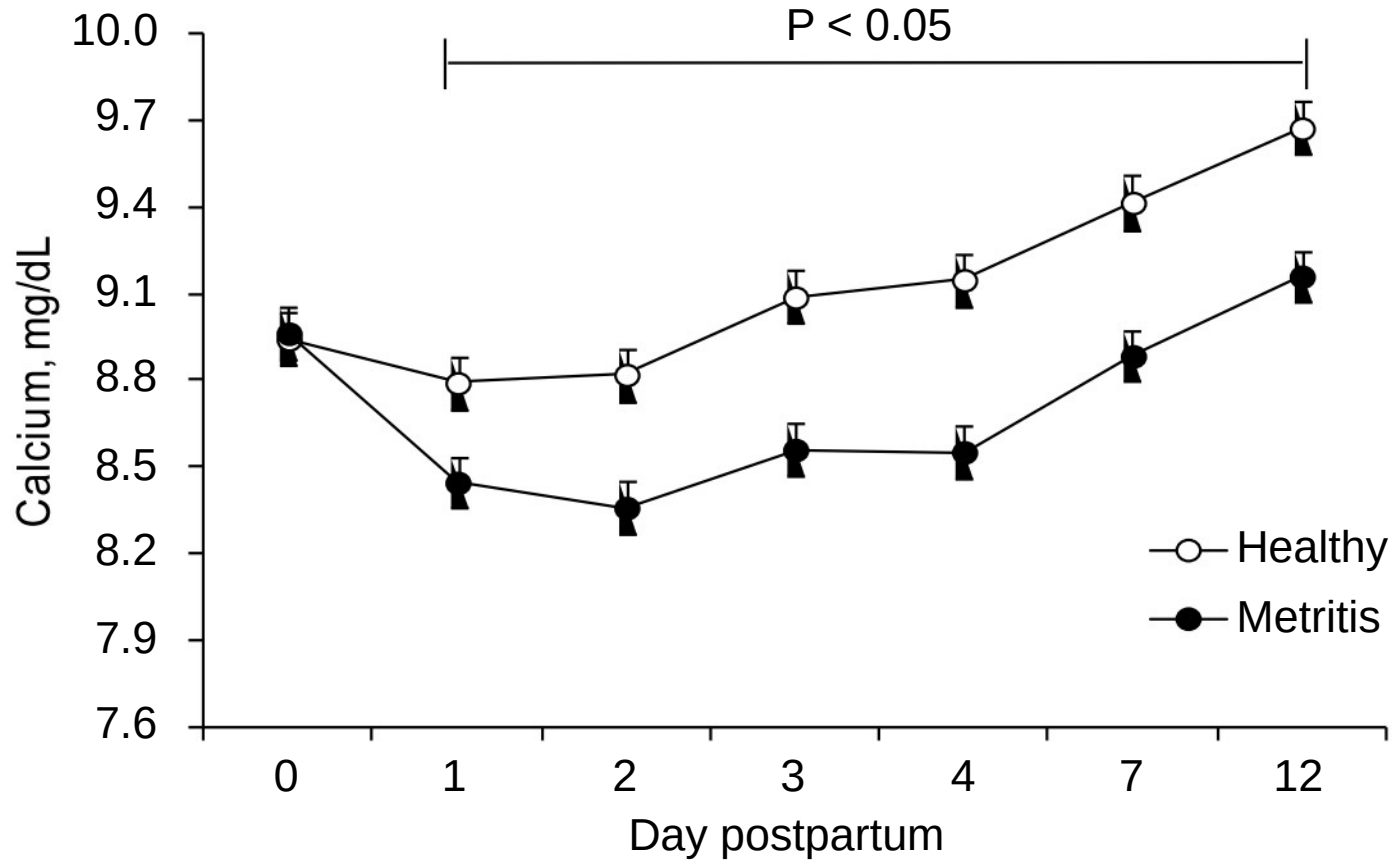
SCHCa and Immune Function





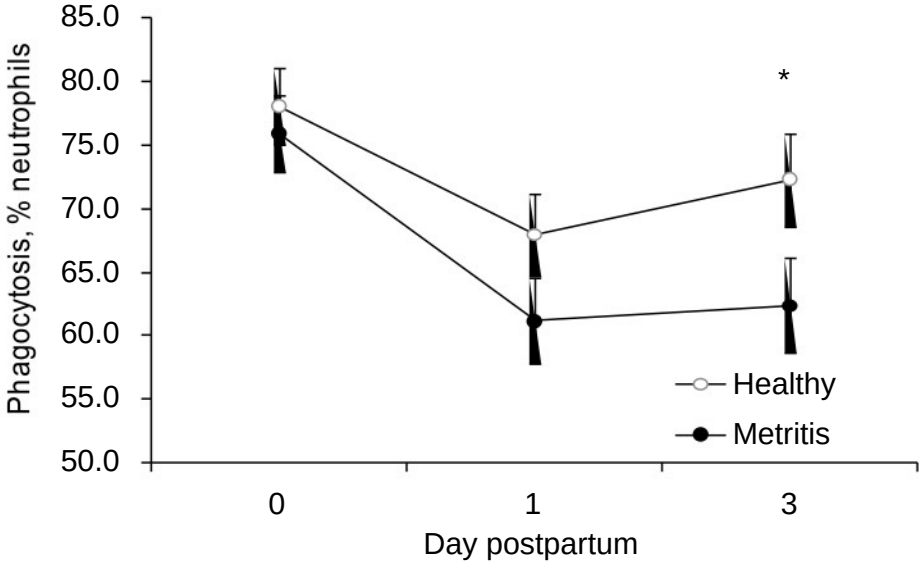
Martinez et al., 2012; JDS

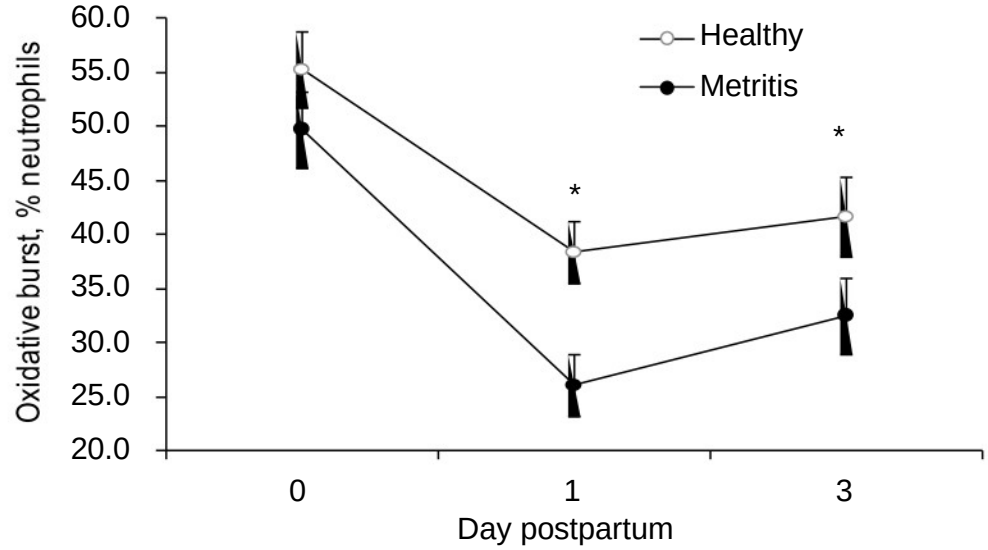
Calcium and Metritis



Martinez et al., 2012; JDS

Metritis and Immune Function





Martinez et al., 2012; JDS

Incidence of Metritis according to Risk Group and Calcium Status

	Risk group[1]			
	Low		High	
Serum Ca,[2] mg/dL	> 8.59	≤ 8.59	> 8.59	≤ 8.59
Metritis,[3,*,¶] % (n/n)	14.3 (4/28)	40.7 (11/27)	20.0 (2/10)	77.8 (35/45)
Puerperal metritis,[4,*] % (n/n)	0.0 (0/28)	29.6 (8/27)	10.0 (1/10)	53.5 (24/45)

* Effect of subclinical hypocalcemia (P < 0.05).

¶ Effect of metritis risk (P < 0.05).

1 Risk group: Low= normal calving; High= cows diagnosed with dystocia, twin, stillbirth, or retained fetal membranes.

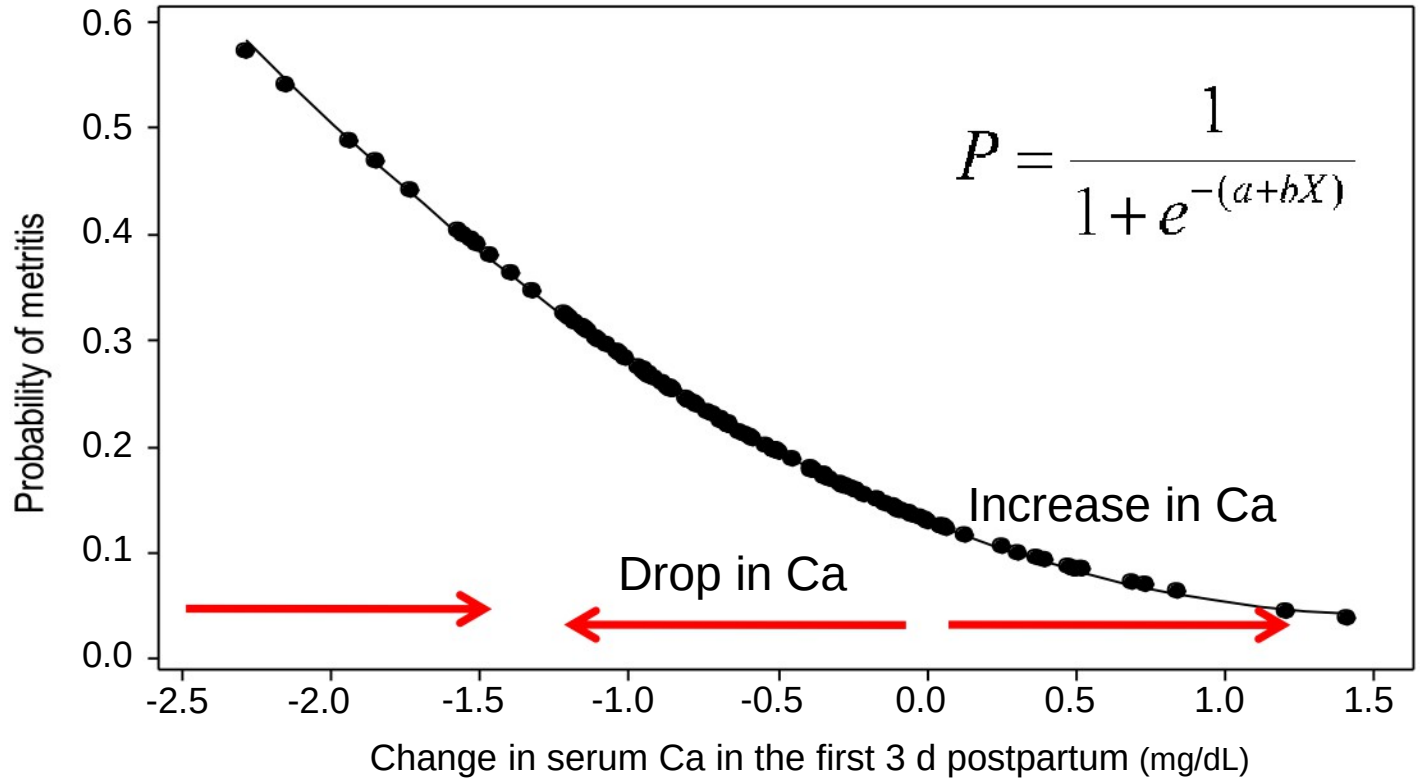
2 Serum Ca concentration in the first 3 d postpartum.

3 Cows with watery fetid vaginal discharge within the first 12 DIM regardless of rectal temperature.

4 Cows with watery fetid vaginal discharge within the first 12 DIM concurrent with rectal temperature ≥ 39.5 ^{o}C.

Martinez et al., 2012; JDS

Probability of Metritis Relative to the Change in Serum Calcium



Effect of change in serum calcium: $P < 0.05$

AOR = 0.38 (95% CI = 0.16 to 0.90); 62% decrease in incidence for each 1 mg/dL increase in Ca

Martinez et al., 2012; JDS

Population Attributable Risk due to Subclinical Hypocalcemia

Metritis

$$PAR = \frac{\text{Incidence of metritis in the study population} - \text{Incidence of metritis in normocalcemic cows}}{\text{Incidence of metritis in the study population}} = \frac{47.3 - 15.8}{47.3} = \mathbf{66.6\%}$$

Puerperal Metritis

$$PAR = \frac{\text{Incidence of puerp. metritis in the study population} - \text{Incidence of puerp. metritis in normocalcemic cows}}{\text{Incidence of puerperal metritis in the study population}} = \frac{30.0 - 2.5}{30.0} = \mathbf{91.7\%}$$

Martinez et al., 2012; JDS

Road to disaster

- Characterized by:
  - High stress/calving/heat
  - Decrease in DMI
  - Low glucose
  - High fat mobilization
  - Sub. ketosis (~40%)
  - Sub. hypocalcemia (25-45%)
  - Immunosuppression

Summary

- Immunosuppression peripartum is a major contributor to high incidence of disease.
- Strategies to maintain DMI and Ca status should help reduce the incidence of disease
  - Focus on cow comfort and access to feedbunk pre- and postpartum
  - Well managed acidogenic diets reduce the incidence of clinical hypocalcemia < 5% but SCH still a challenge.

Cow Comfort

Can we do anything else to help?

Flunixin Meglumine to Prevent Disease

FM treatment for 1-3 days post-calving:

- Increased risk of retained placenta 2.5X (Waelchli et al., 1999; Vet. Rec.; Duffield, et al., 2009; JDS Abstr.)
- Increased risk of metritis 1.5X (Duffield, et al., 2009; JDS Abstr.)
- Increased body temperature (Shwartz et al., 2009; JDS)
- Decreased DMI, milk yield and EB (Shwartz et al., 2009; JDS) in the first week

PPG for cows with BHB ≥ 1.2 mmol/L

Table 1. Cox proportional models showing hazard ratios (HR) for 741 Holstein cows with at least one positive test for subclinical ketosis from 3 to 16 DIM randomly assigned to propylene glycol treatment (n = 372) or control (n = 369)

Event[1]	Estimate	SE[2]	*P*-value[3]	HR	95% CI[4]
BHBA <1.2 m*M*/L	0.41	0.091	<0.001	1.50	1.26 to 1.79
BHBA ≥3.0 m*M*/L	0.62	0.24	0.009	0.54	0.34 to 0.86

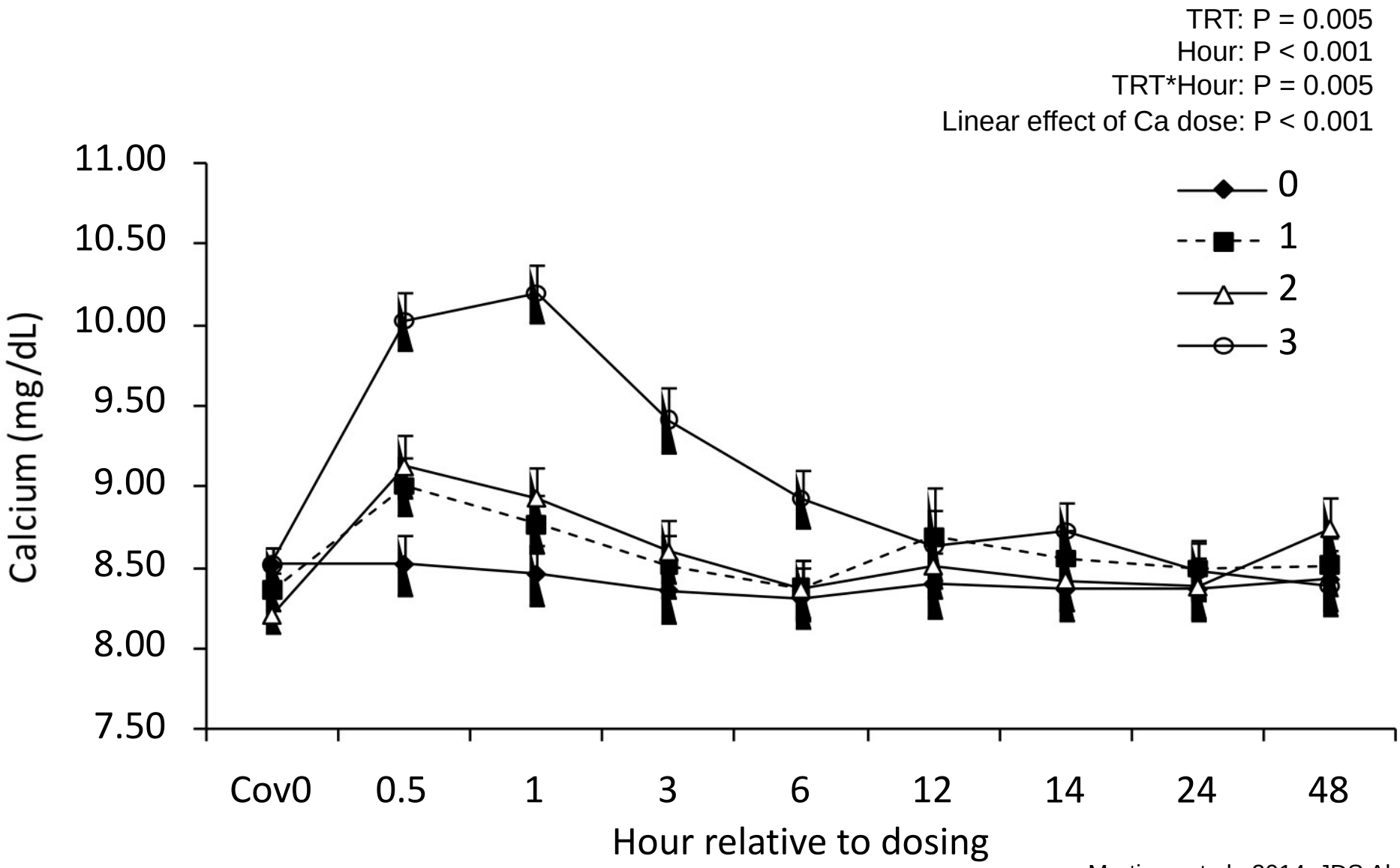
Table 4. Estimates for 3 final Poisson regression models showing risk ratios (RR) for 741 Holstein cows with at least 1 positive test for subclinical ketosis from 3 to 16 DIM randomly assigned to propylene glycol treatment (n = 372) or control (n = 369)[1]

Model	Estimate	SE[2]	*P*-value[3]	RR	95% CI[4]
DA	0.47	0.11	<0.0001	1.6	1.3 to 2.0
CULL	0.72	0.29	0.01	2.1	1.2 to 3.6
PREG	0.27	0.09	0.002	1.3	1.1 to 1.5

[1]The 3 outcomes modeled were 1) development of a displaced abomasum (DA) within 30 DIM, 2) removal from herd (CULL) within 30 DIM, and 3) conception to first service (PREG).

McArt et al., 2011; JDS

Calcium bolus - CaCl2 + CaSO4



Martinez et al., 2014; JDS Abstr

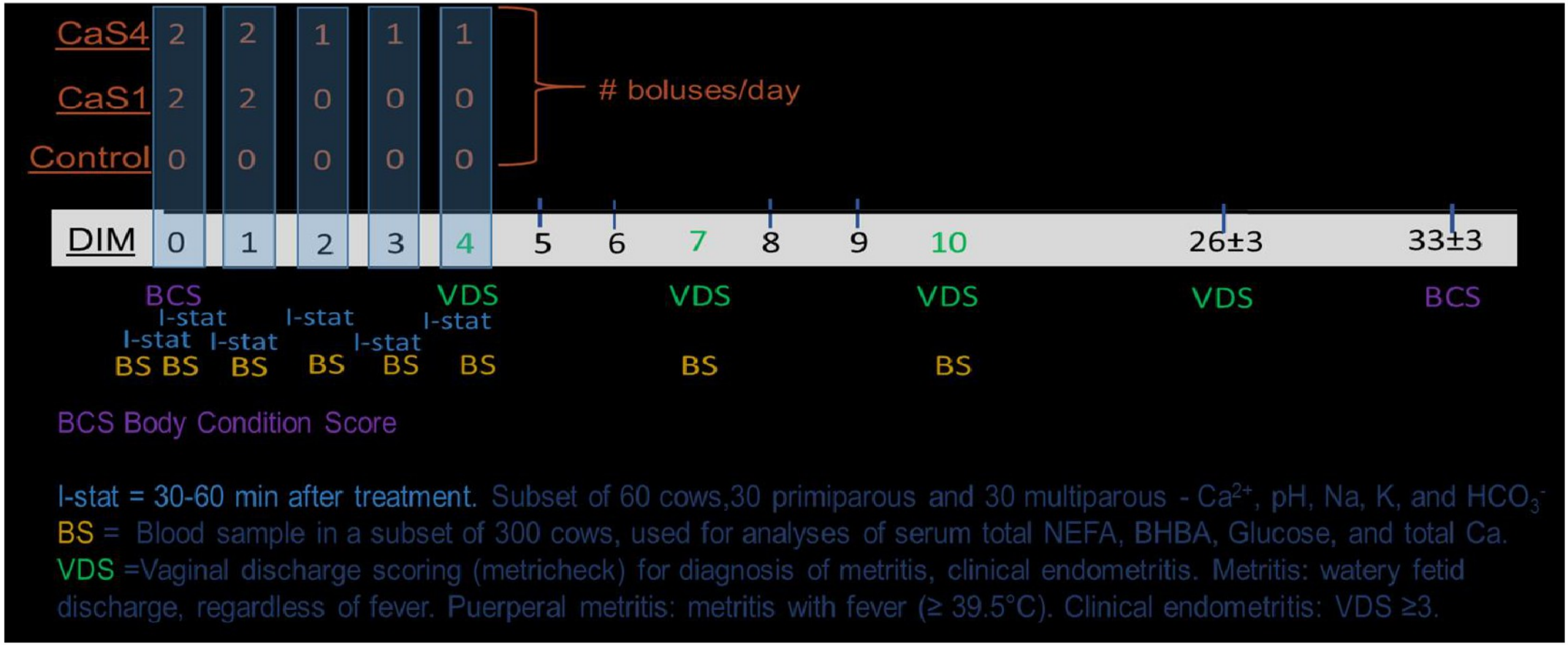
J. Dairy Sci. 95:7051–7065
http://dx.doi.org/10.3168/jds.2012-5510

Effect of oral calcium bolus supplementation on early-lactation health and milk yield in commercial dairy herds

G. R. Oetzel*[1] and B. E. Miller†
*School of Veterinary Medicine, University of Wisconsin, Madison 53706
†Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO 64506

- Ca bolus administered at calving and 8-35h later.
- No effect in Ca concentration 8-35 h after TRT.
- No effect in disease incidence: metritis, mastitis, pneumonia, death or culling.
- No overall effect on milk yield or reproduction.
- Increased in the first postpartum milk test in cows with previous 305ME above average (≥ 105) and lame cows.

Calcium Bolus



Martinez et al., 2014; JDS Abstr.

Calcium Bolus

	High Risk of Metritris			Low Risk of Metritris			
	Control	CaS1	CaS4	Control	CaS1	CaS4	SEM
Ca^{2+}, mM [1,*¶]	1.08	1.15	1.21	1.09	1.17	1.20	0.02
Temperature, ˚C	38.87	38.90	38.90	38.76	38.77	38.74	0.03
Milk, Kg/d, first 7DIM	29.4	29.4	27.7	32.9	30.7	32.1	1.10
Glucose, mg/dL [2]	53.8	53.7	53.3	57.3	53.9	55.7	0.02
BHBA, mM [2]	0.90	0.90	0.85	0.76	0.88	0.83	0.04
NEFA, mM [2]	0.536	0.597	0.588	0.545	0.601	0.581	0.03

Martinez et al., 2014; JDS Abstr.

Calcium Bolus

	High Risk of Metritris			Low Risk of Metritris		
	Control	CaS1	CaS4	Control	CaS1	CaS4
Metritis [1,*]	55.4 (41/74)	63.5 (47/74)	56.2 (41/73)	9.5 (7/74)	20.3 (15/74)	20.3 (15/74)
PuMet [2]	23.0 (17/74)	25.7 (19/74)	25.7 (19/74)	2.7 (2/74)	5.4 (4/74)	9.5 (7/74)
Endometritis [3]	38.2 (26/68)	33.8 (24/71)	31.4 (22/70)	22.2 (16/72)	21.9 (16/73)	18.1 (13/72)
Ketosis [4]	8.1 (6/74)	5.5 (4/73)	2.8 (2/71)	4.2 (3/72)	8.2 (6/73)	8.1 (6/74)
SCKet [5]	43.2 (32/74)	43.8 (32/73)	33.8 (24/71)	23.0 (17/74)	32.4 (24/74)	28.4 (21/74)

Martinez et al., 2014; JDS Abstr.

Cure rate using Dextrose or Excede

Table 2. Prevalence (%) of clinical endometritis (CE) at exam 2 (40 ± 3 DIM) in lactating Holstein cows using vaginoscopy scoring technique and measurement of cervical diameter by ultrasonography

	Exam 2[1]			
Parameter	CON (n = 83)	DEX (n = 79)	CCFA (n = 75)	*P*-value
Clinical uterine discharge				
0 (clear mucus)	24.53[b]	44.68[a]	41.30[a]	0.02
1 (mucus with flecks of pus)	33.96	27.66	21.74	
2 (mucopurulent)	32.08	21.28	28.26	
3 (brown-red foul)	9.43	6.38	8.70	
Cervical diameter (cm)				
<4	62.50	66.02	65.79	
4.0–5.0	31.25	29.10	23.68	
≥5.1	6.25	4.88	10.53	

[a,b]Values with different superscript letters within a row differ significantly at $P < 0.05$.

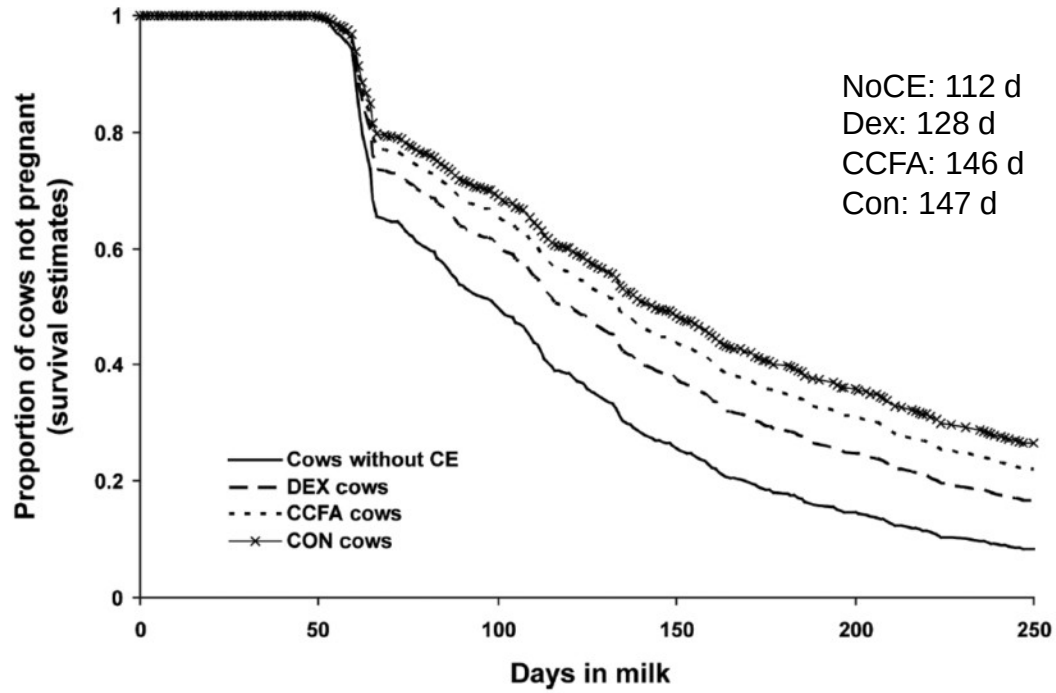
Brick et al., 2012; JDS

Pregnancy per AI for First Services

Table 6. Proportions (%) of pregnancies per AI (P/AI) in lactating Holstein cows with clinical endometritis (CE) following an intrauterine dextrose infusion (DEX), ceftiofur crystalline free acid (CCFA), or untreated animal (CON)[1]

	Cows with CE				
Variable	CON (n = 83)	DEX (n = 79)	CCFA (n = 75)	Cows without CE (n = 523)	*P*-value
First-service P/AI for cows with CE only[2] (%)	21.1 ± 4	29.8 ± 4	19.7 ± 4	—	0.1
First-service P/AI for all cows[3] (%)	20.1 ± 4^{b}	30.5 ± 5^{ab}	19.4 ± 4^{b}	39.1 ± 2^{a}	0.0001
Pregnancy loss[4] (%)	11.6 ± 5^{a}	9.1 ± 4^{ab}	13 ± 5^{a}	5.8 ± 2^{b}	0.03

[a,b]Values with different superscript letters within a row differ significantly at $P < 0.05$.



Brick et al., 2012; JDS

Summary

- Use NSAIDs judiciously; no blanket TRT
- 300 ml of PPG to cows with BHB ≥ 1.2 mmol/L helped treat SCK and prevent clinical ketosis and the downstream negative effects on fertility
- Supplementation with Ca bolus gave controversial results. Maybe there is a benefit in milk yield for a group of cows but health is either unchanged or negatively affected.
- Dextrose is a promising TRT for CE

Conclusion

- Initiation of lactation leads to decreases in concentrations of plasma glucose, glycogen and calcium, and leads to increases in NEFA and BHBA.
- NEFA, BHBA, and low calcium directly affect immune function.
- Immunosuppression during periods of NEB predisposes cows to postpartum diseases.
- Postpartum diseases affect pregnancy and PL.
- There is no magic bullet.

Questions???