LIPID SUPPLEMENTATION AND HEPATIC METABOLISM IN RELATION TO HEALTH AND FERTILITY

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Results Beyond Education

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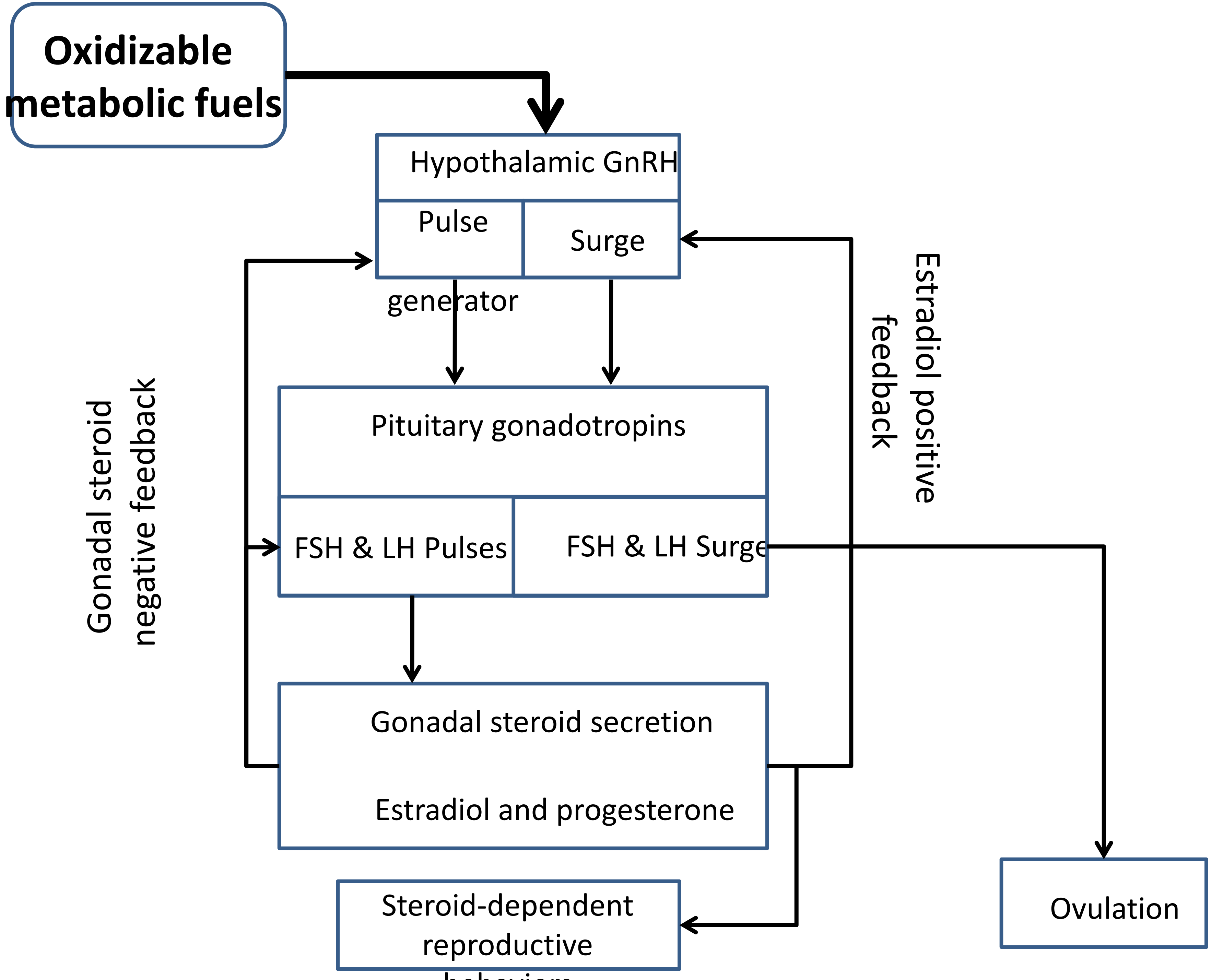
DAIRY SCIENCE RESEARCH

Scope of Presentation

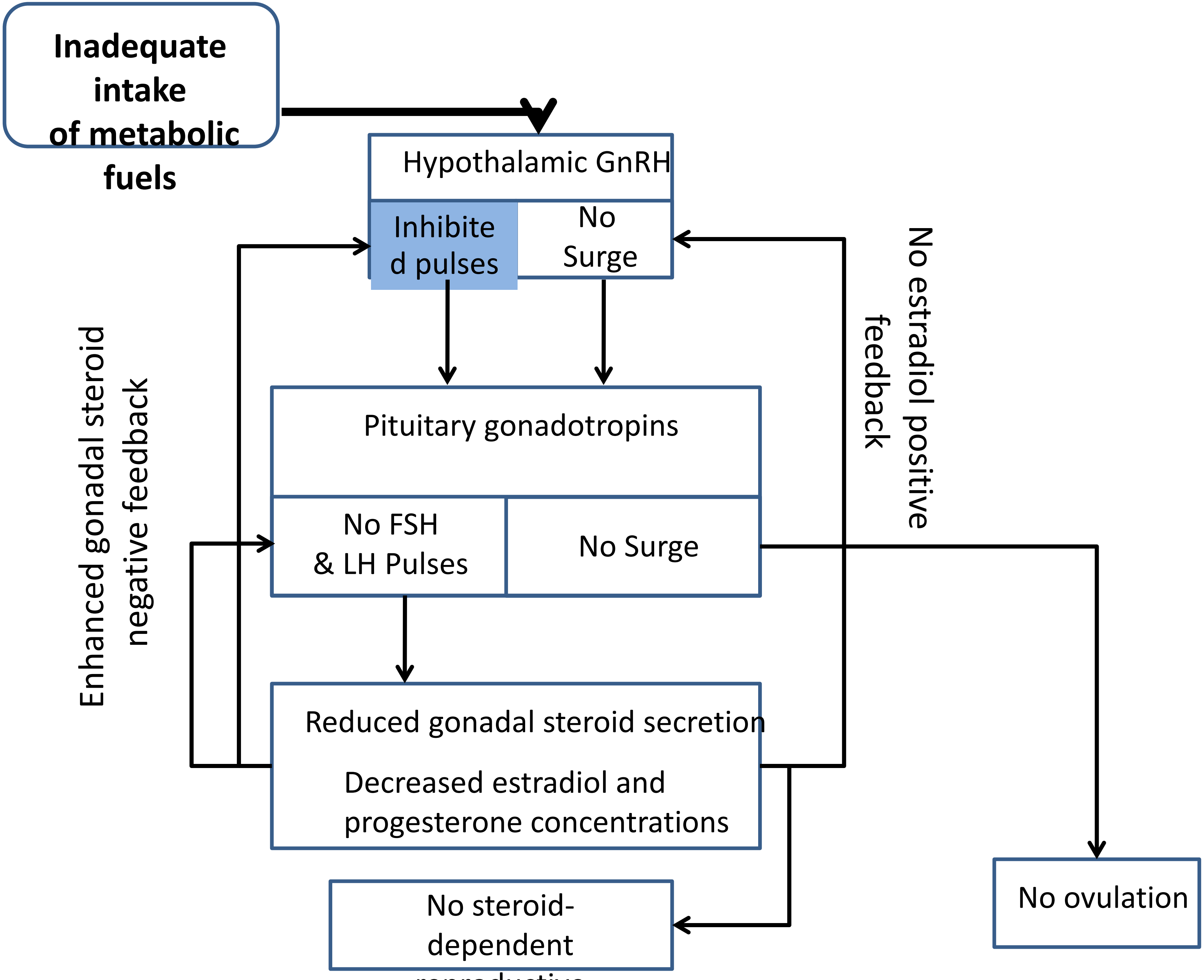
- Control of reproduction in mammals
  - ✓ The example of the high-producing dairy cow

- Link between intermediary metabolism, liver health, and reproduction

- The role of dietary fatty acids on hepatic metabolism, production and reproduction



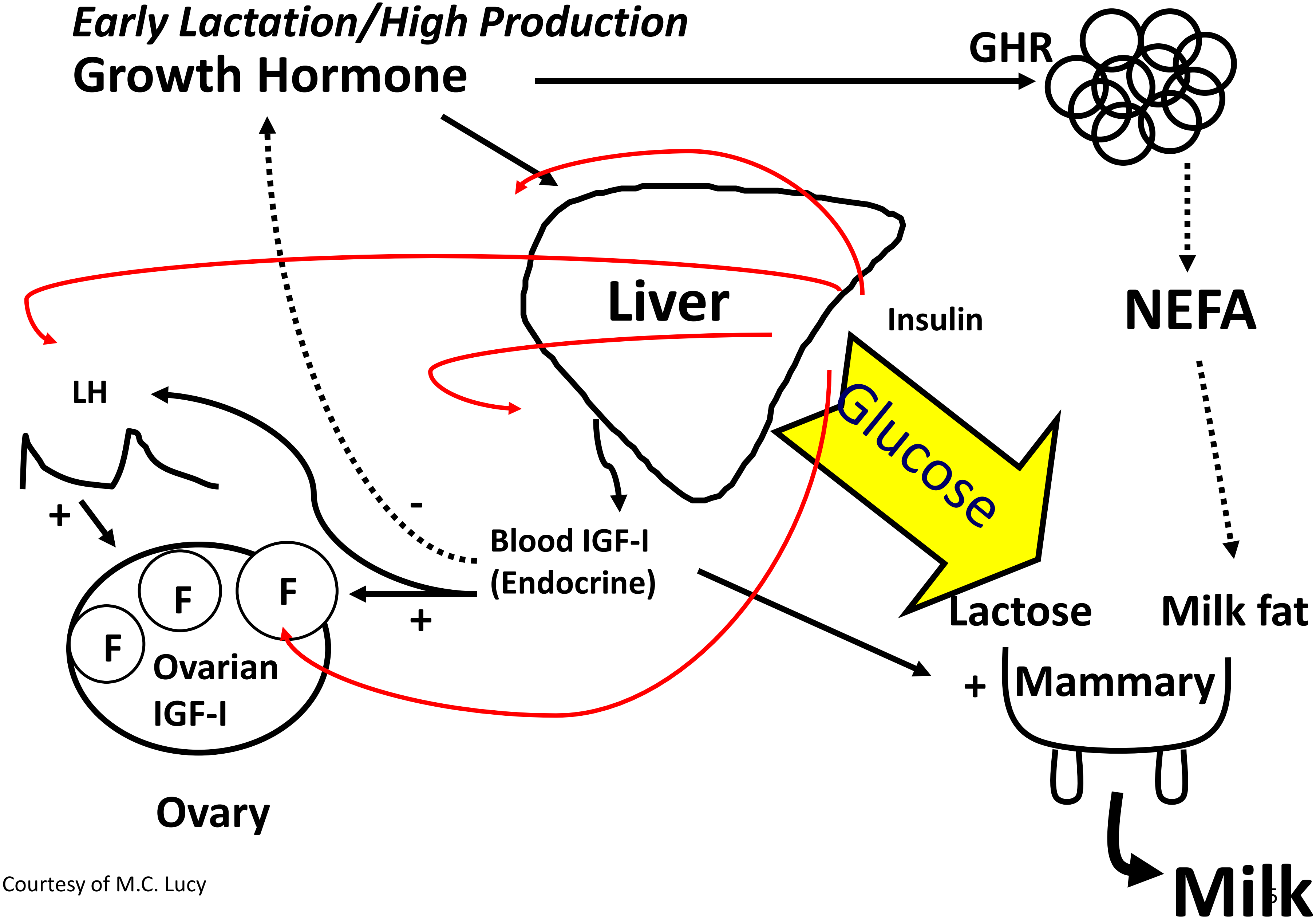
Oxidizable metabolic fuels
Hypothalamic GnRH
Pulse generator
Surge
Estradiol positive feedback
Gonadal steroid negative feedback
Pituitary gonadotropins
FSH & LH Pulses
FSH & LH Surge
Gonadal steroid secretion
Estradiol and progesterone
Steroid-dependent reproductive
Ovulation



Inadequate intake of metabolic fuels
Hypothalamic GnRH
Inhibited pulses
No Surge
Pituitary gonadotropins
No FSH & LH Pulses
No Surge
Enhanced gonadal steroid negative feedback
No estradiol positive feedback
Reduced gonadal steroid secretion
Decreased estradiol and progesterone concentrations
No steroid-dependent
No ovulation

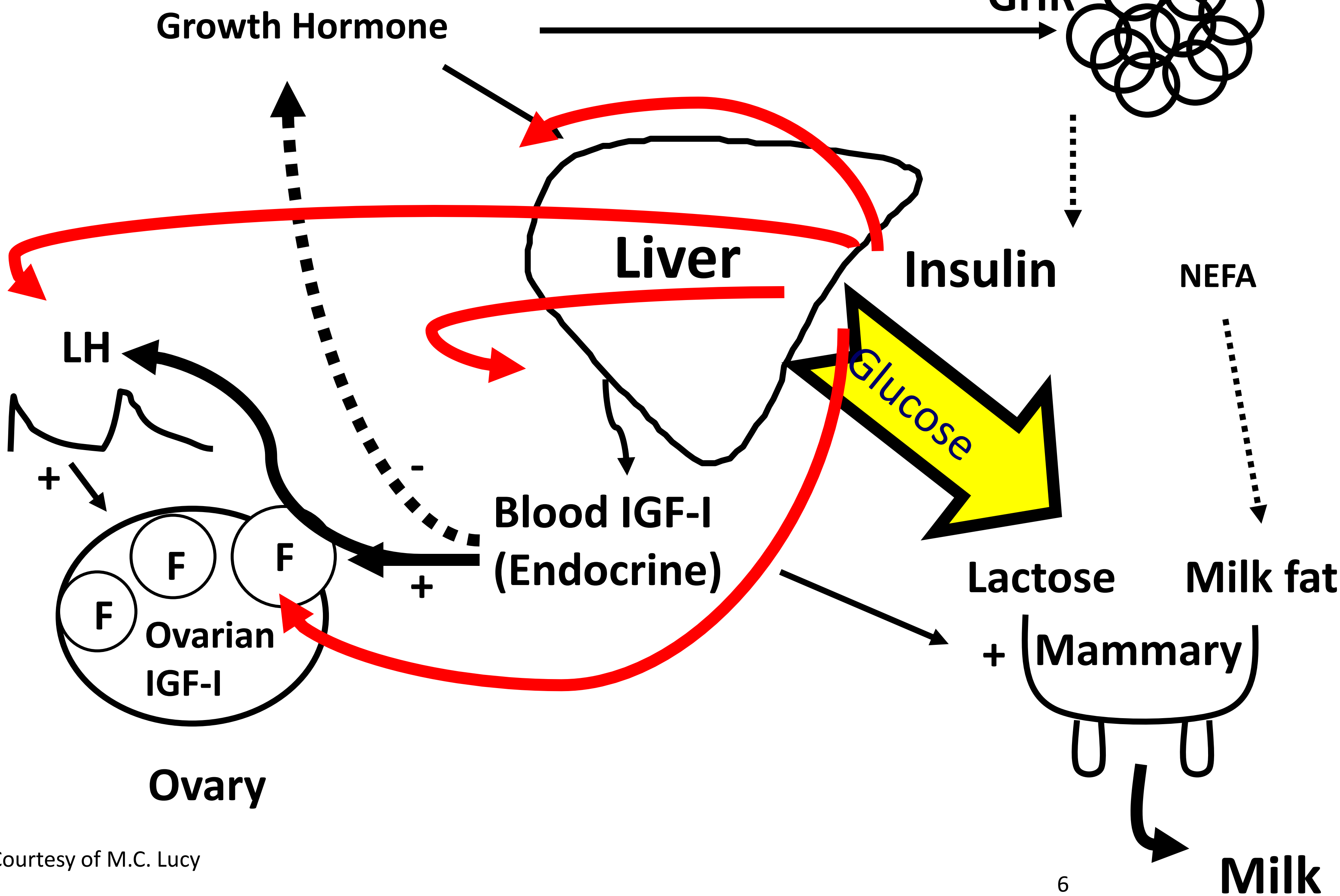
Nutrient Partitioning in Dairy Cows

Early Lactation/High Production



Courtesy of M.C. Lucy

Nutrient Partitioning in Dairy Cows
Late Lactation/Low Production



Courtesy of M.C. Lucy

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Movies

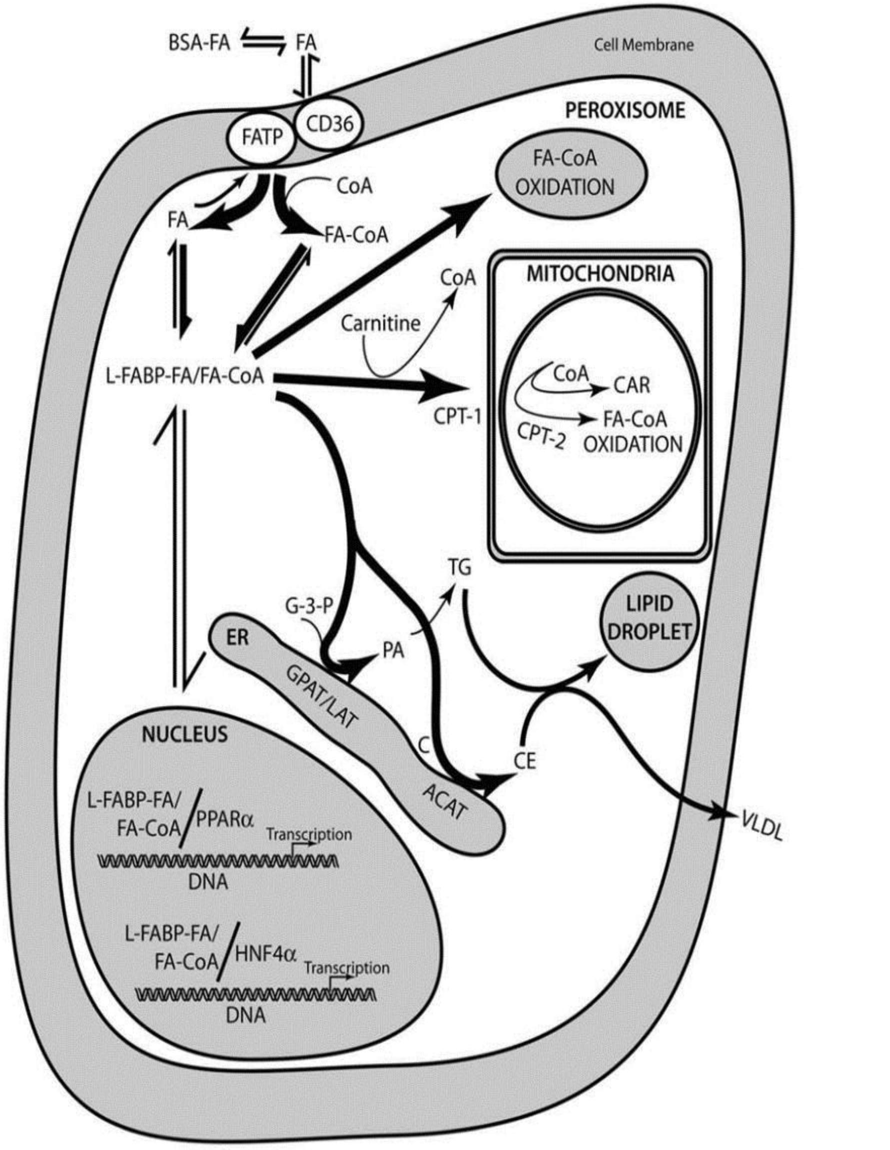
Aggressive Feeding Behavior

Selective Shy Feeding Behavior

Industry Standards for Space and Comfort Oftentimes Are Inadequate for Transition Cows

Fatty Liver and Ketosis

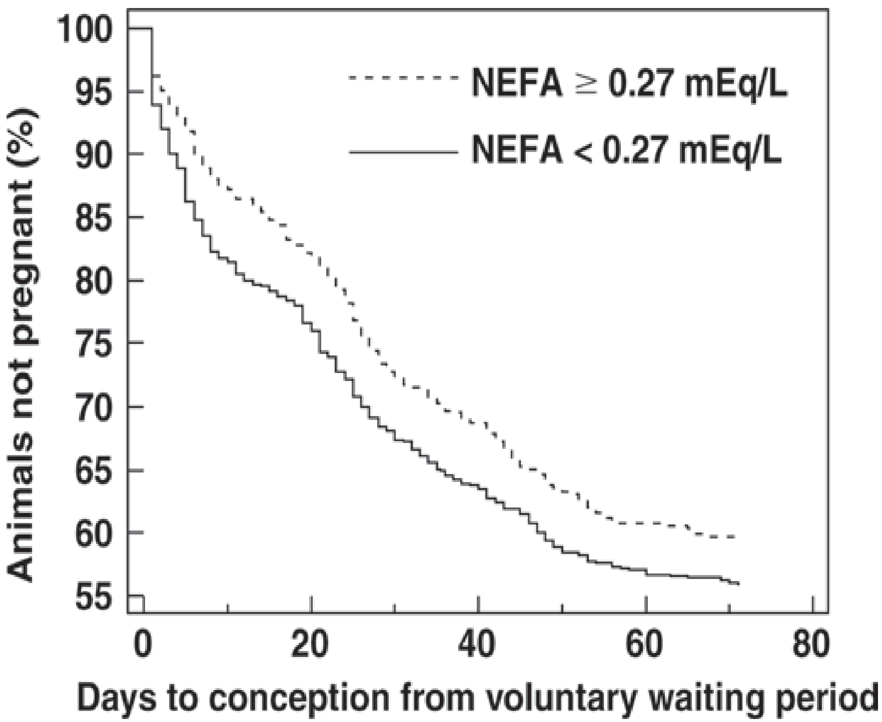
- At 11 DIM
- Plasma NEFA of 0.36 mM
- Bovine liver extracted 2.78 M of NEFA/day
- If one assumes palmitate, then:
  - 2.78 x 256 = 713 g of NEFA extracted by the liver per day
  - Bovine liver weighs 8 to 10 kg wet weight (4 to 6 kg DM)
- Extractions would be much greater at higher NEFA around calving (1 mM)

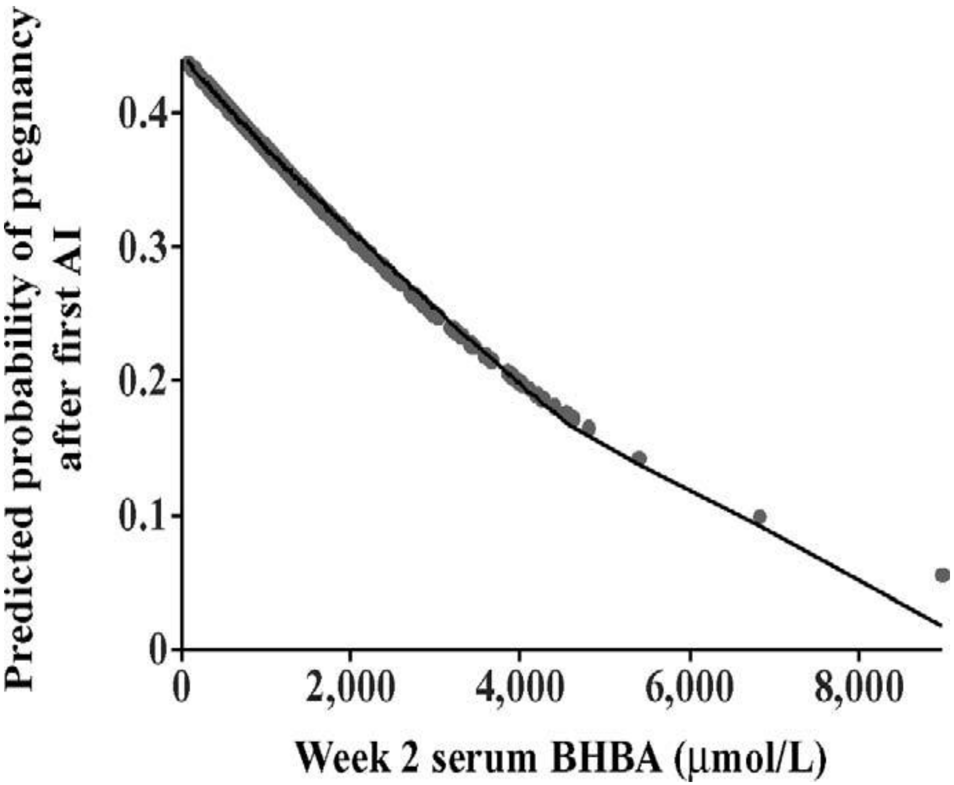


Reynolds et al. (2003) J. Dairy Sci. 86:1201–1217

Atshaves, B.P, J. Nutr. Biochem. (2010) 21: 1015–1032.

Energy Metabolism During the Transition Period is Associated with Fertility

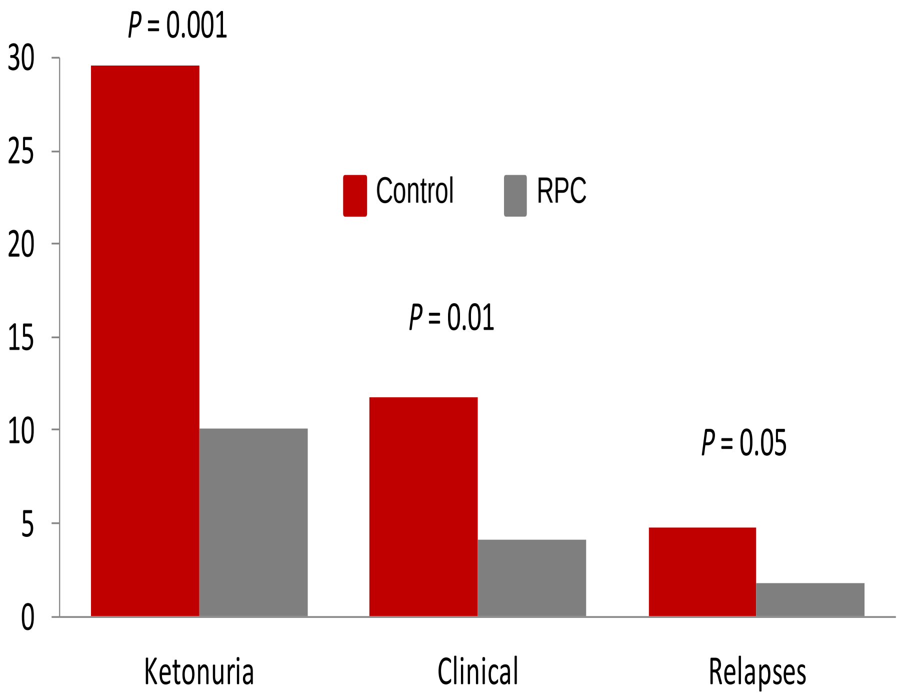




Ospina et al. (2010) J. Dairy Sci. 93:1596-1603

Walsh et al. (2007) J. Dairy Sci. 90:2788-279

Effect of Rumen-Protected Choline on Clinical Ketosis and Fatty Liver



	Treatment		
	Control	RPC	
DM, %	54.7 ± 3.0	60.1 ± 3.3	0.23
Glycogen			
As is, %	0.94 ± 0.15	1.14 ± 0.16	0.36
DM, %	2.01 ± 0.36	2.20 ± 0.40	0.72
Triacyglycerol			
As is, %	5.86 ± 1.17	4.08 ± 1.29	0.31
DM, %	10.39 ± 1.73	6.02 ± 1.89	0.10
Hepatic lipidosis[1], %	40.0 (10/25)	14.3 (3/21)	0.05

Lima et al. (2012) Vet. Journal 193:140-145

Health Problems in the First 60 DIM and Pregnancy in Dairy Cows

Category	Pregnant, %	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

5,719 postpartum dairy cows evaluated daily for health disorders in seven dairy farms in the US

Santos *et al.* (2010) Soc. Reprod. Fertil. 67:387-403

Impact of Clinical Diseases on Proportion of Single Ovulating Dairy Cows with Embryo/Oocytes as Embryos Grades 1 & 2

Health problem (n = 476)	% of cows	Grades 1 & 2, %	AOR (95% CI)	P
Healthy	56.3	61.6	1.00	
Clinical disease	43.7	46.3	0.54 (0.35-0.84)	<0.01
Multiple diseases	24.3	42.4	0.52 (0.30-0.89)	0.02
Type of clinical disease				
Healthy	56.3	61.6	1.00	
Uterine disease	18.9	36.5	0.39 (0.22-0.68)	<0.01
Ketosis	11.1	31.3	0.33 (0.15-0.72)	<0.01
Mastitis	21.6	50.0	0.76 (0.44-	0.34

Bisinotto *et al.* (2012) Anim. Reprod. 9:260-272

Impact of Clinical Diseases on Proportion of Single Ovulating Dairy Cows with Embryos as Embryos Grades 1 & 2

Health problem (n = 476)	% of cows	Grades 1 & 2, %	AOR (95% CI)	P
Healthy	56.3	71.8	1.00	
Clinical disease	43.7	59.1	0.57 (0.34-0.94)	0.03
Multiple diseases	24.3	56.0	0.56 (0.30-1.05)	0.07
Type of clinical disease				
Healthy	56.3	71.8	1.00	
Uterine disease	18.9	50.0	0.42 (0.22-0.80)	<0.01
Ketosis	11.1	40.0	0.29 (0.12-0.67)	<0.01
Mastitis	21.6	63.3	0.82 (0.43-	0.54

Bisinotto *et al.* (2012) Anim. Reprod. 9:260-272

Impact of Clinical Diseases on Pregnancy on Day 15 after AI in Lactating Dairy Cows

Health problem (n = 145)	% of cows	Pregnant, %	AOR (95% CI)	P
Healthy	61.4	49.3	1.00	
Clinical disease	38.6	29.8	0.44 (0.20-0.94)	0.03
Multiple diseases	15.2	31.6	0.59 (0.21-1.69)	0.32
Type of clinical disease				
Healthy	61.4	49.4	1.00	
Uterine disease	12.4	20.0	0.31 (0.10-1.10)	0.06
Mastitis	11.7	35.7	0.75 (0.24-2.38)	0.62

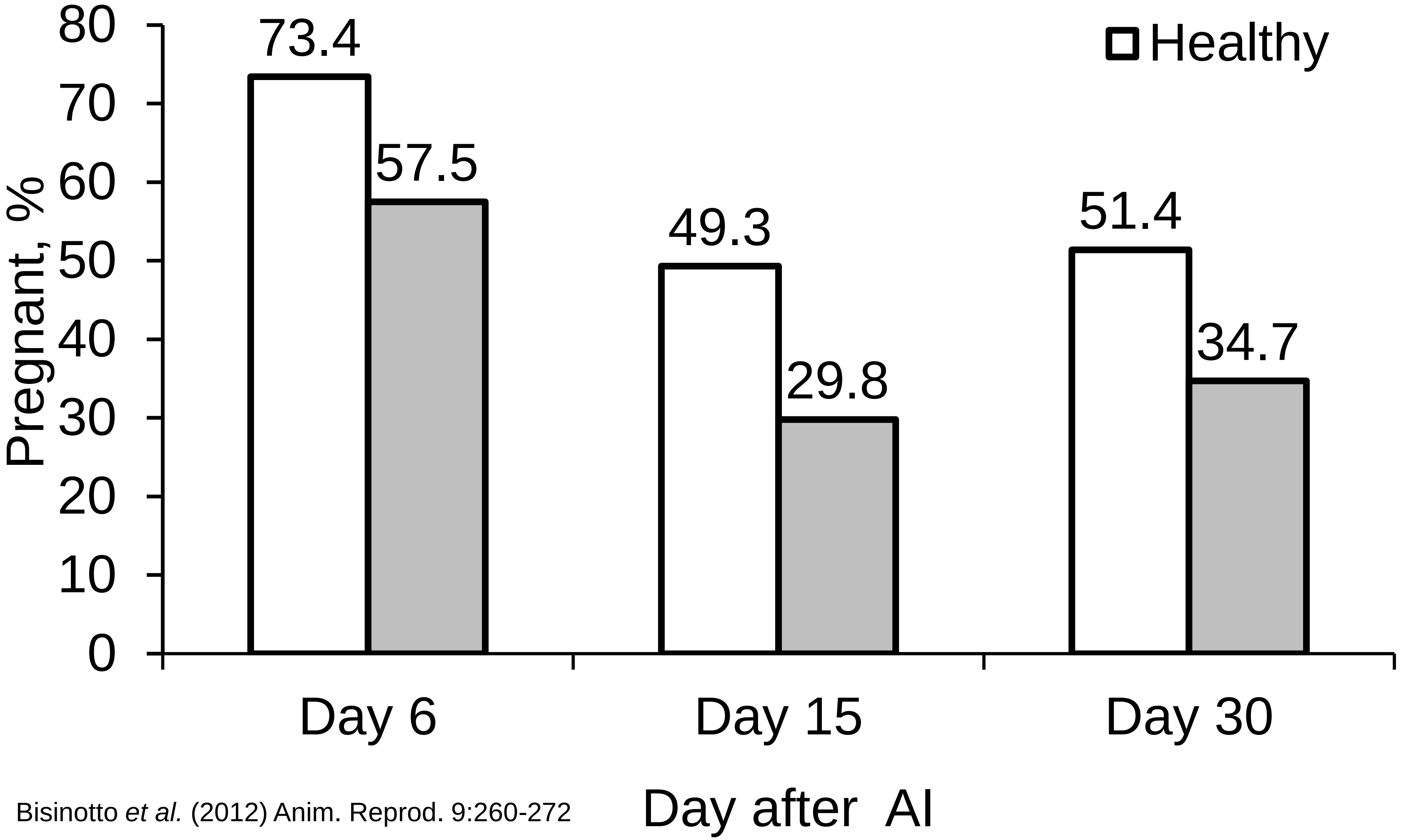
Bisinotto *et al.* (2012) Anim. Reprod. 9:260-272

Impact of Clinical Diseases on Percentage of Embryos as Elongated Embryos on Day 15 after AI in Lactating Dairy Cows

Health problem (n = 145)	% of cows	Elongated, %	AOR (95% CI)	P
Healthy	61.4	83.9	1.00	
Clinical disease	38.6	28.6	0.10 (0.02-0.35)	<0.01
Multiple diseases	15.2	16.7	0.10 (0.07-0.66)	<0.01
Type of clinical disease				
Healthy	61.4	83.9	1.00	
Uterine disease	12.4	0.0	0.05 (0.01-0.30)	<0.01
Mastitis	11.7	40.0	0.29 (0.04-1.93)	0.19

Bisinotto *et al.* (2012) Anim. Reprod. 9:260-272

Summary of Estimates of Pregnancy at Different Stages after AI According to Health Status



Bisinotto *et al.* (2012) Anim. Reprod. 9:260-272

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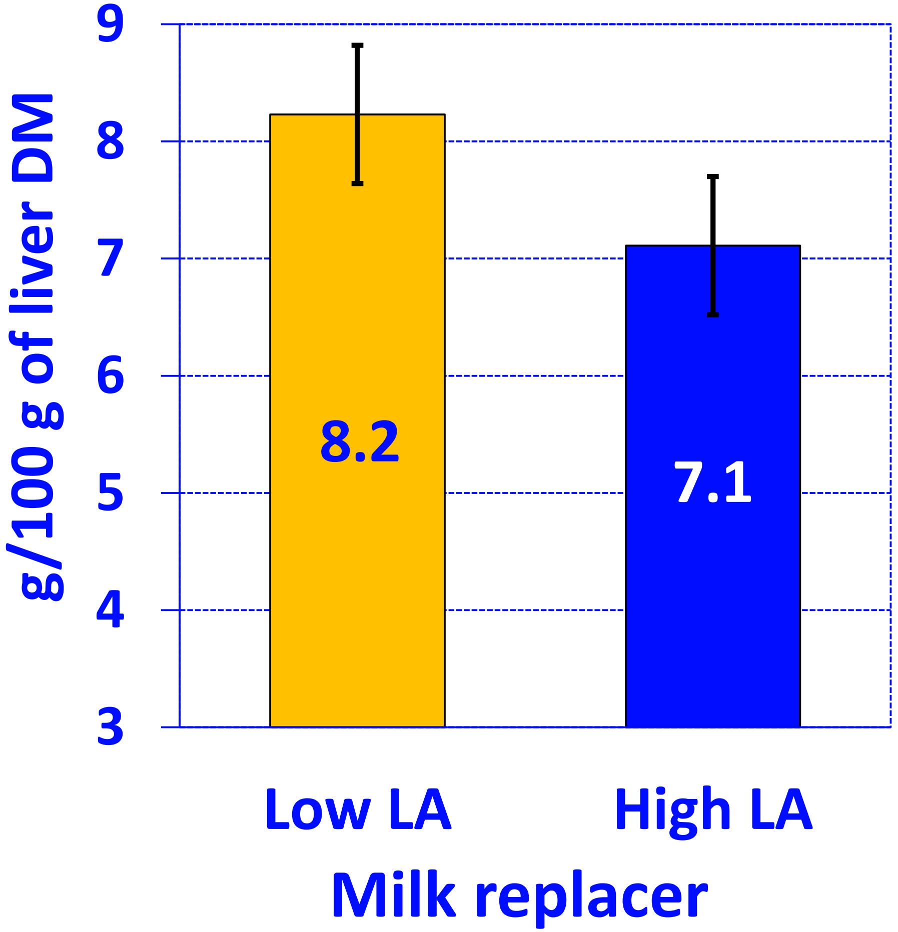
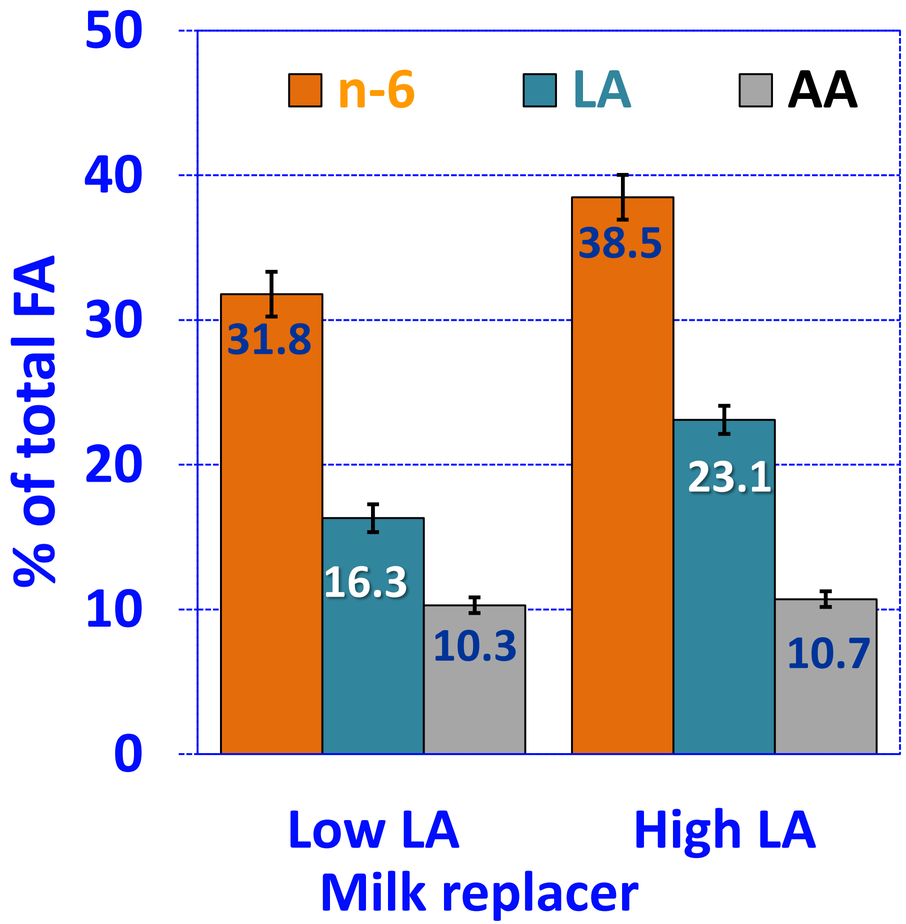
Liver total fatty acids (g/100 g of DM)



Milk replacer, *P* = 0.04

Garcia et al. (2012) J. Dairy Sci. 95 (Suppl. 2):717 (Abstr.).

Liver total omega 6 (n-6), linoleic acid (LA), and arachidonic acid (AA)



n- 6, *P* < 0.01

LA, *P* < 0.01

AA, *P* = 0.36

Up-regulated PPAR Signaling Pathway FAT by Milk Replacer Interaction

Ligand	Transcription factor	Target Gene (37)	Function
Increased intake of linoleic acid early in life	PPAR-α	ACAT1, LCAD, CYP4A*	Fatty acid oxidation
		CYP27A	Cholesterol metabolism
		Apo-A5	Fatty acid transport

- ⬇ BHBA in plasma
- ⬇ Total cholesterol in plasma
- ⬇ Fat concentration in liver

Garcia et al. (2012) J. Dairy Sci. 95 (Suppl. 2):717 (Abs

* 2 subfamilies of CYP4A were up-regulated.

Materials and Methods

- 76 cows blocked by parity (1 vs. > 1) and BCS at dry off and, within block, randomly assigned to 1 of 3 treatments
  - Control (no fat supplementation)
  - Saturated free FA (SFA - Energy Booster)
  - Ca salts of palm and soybean oils (EFA - Megalac R)

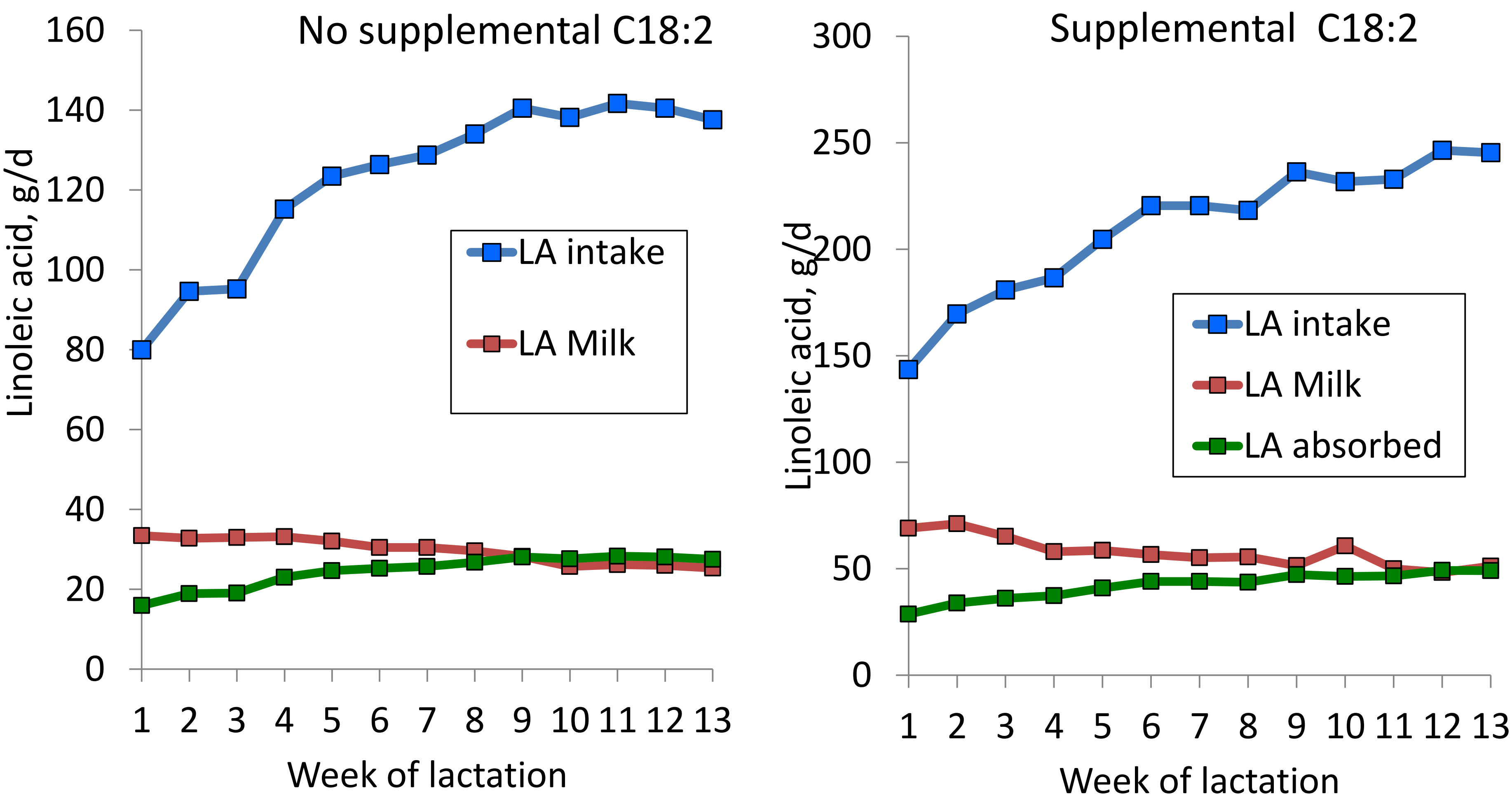
- Cows were fed diets from -50 to + 95 DIM

- Control diet was formulated to contain the least amount of total and essential fatty acids. Lactating diets were low in NDF (30%)
  - SFA and EFA replaced corn grain
  - Fatty acids were supplemented at 1.5% prepartum and 2.0% postpartum

- Lactation performance was evaluated during the first 90 DIM

- Liver tissue was collected at 14 DIM and processed for FA analysis and gene expression by microarray and RT-PCR analyses

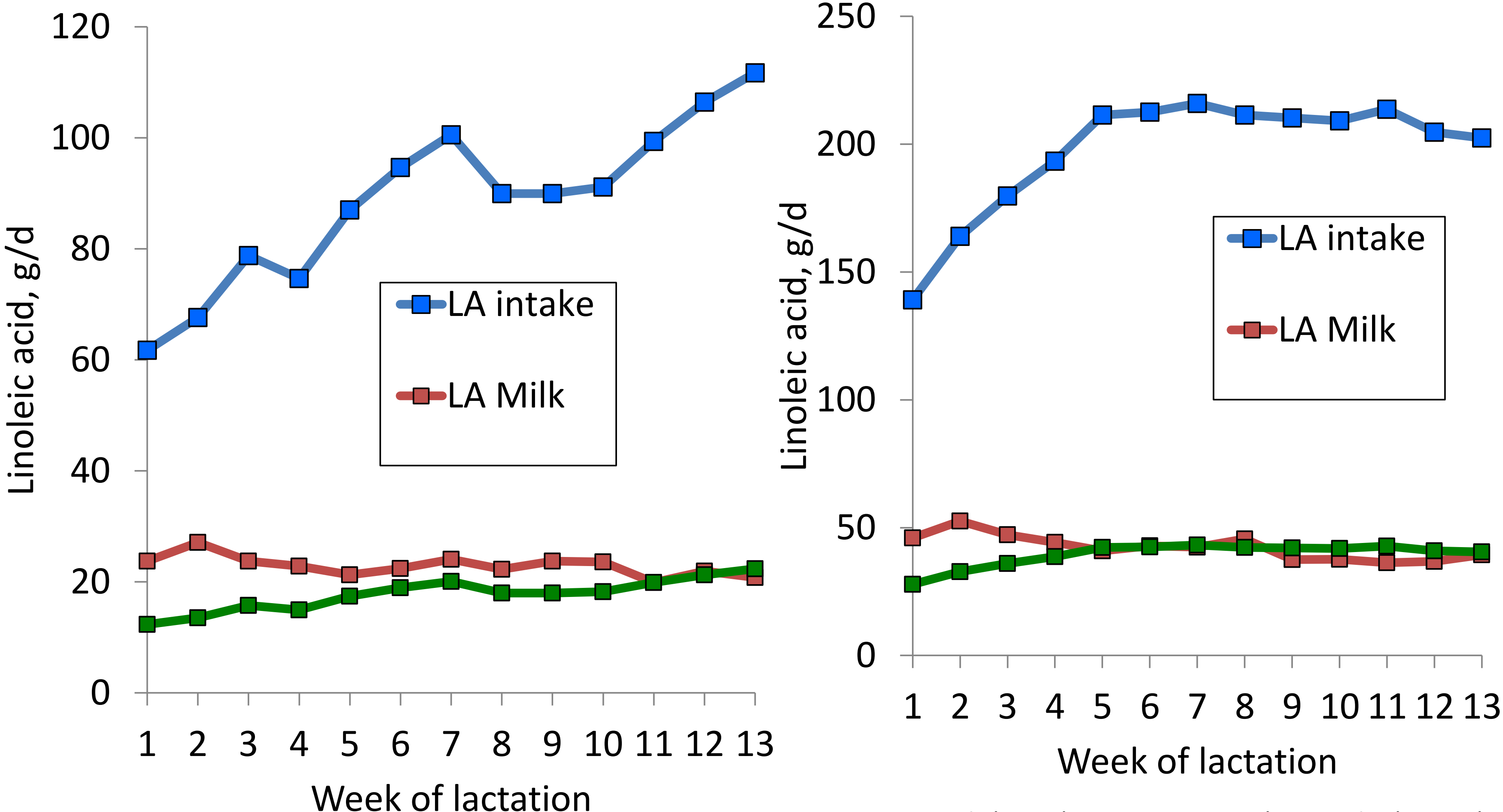
Linoleic Acid (C18:2) "Balance" of Multiparous Cows Fed "Low" C18:2 Diets with or without Supplemental C18:2



Greco et al. (2010) J. Dairy Sci. 93 (E-Suppl. 1): 448 (Abstr

Dietary C18:2: Assigned biohydrogenation of 75% and gut absorption of 80%

Linoleic Acid (C18:2) "Balance" of Primiparous Cows Fed "Low" C18:2 Diets with or without Supplemental C18:2

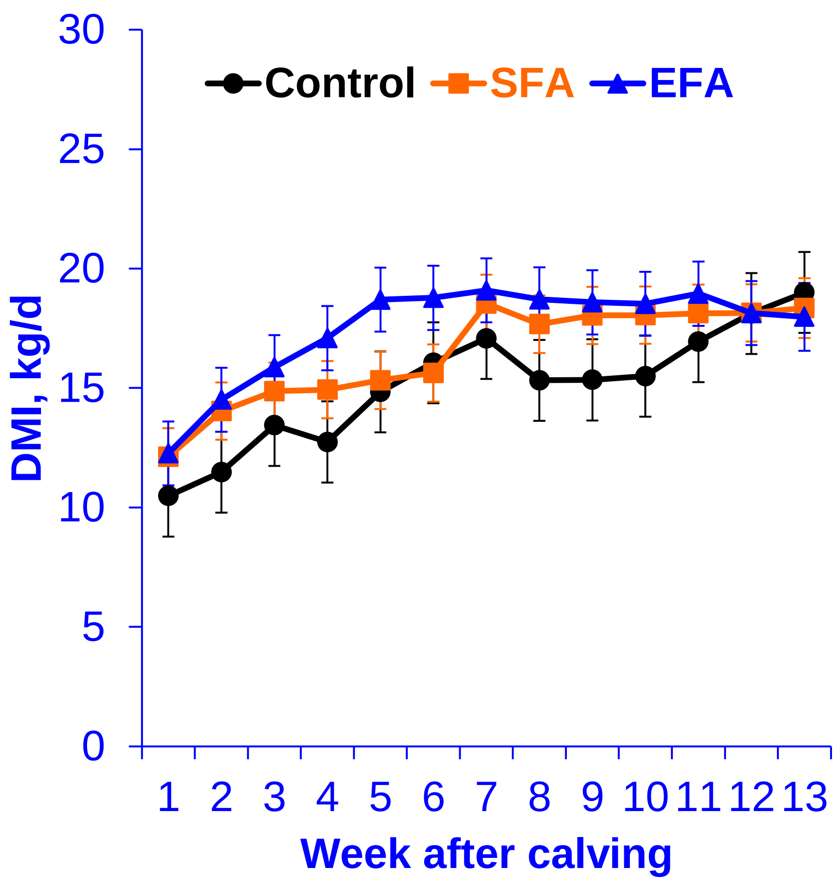


Greco et al. (2010) J. Dairy Sci. 93 (E-Suppl. 1): 448 (Abst

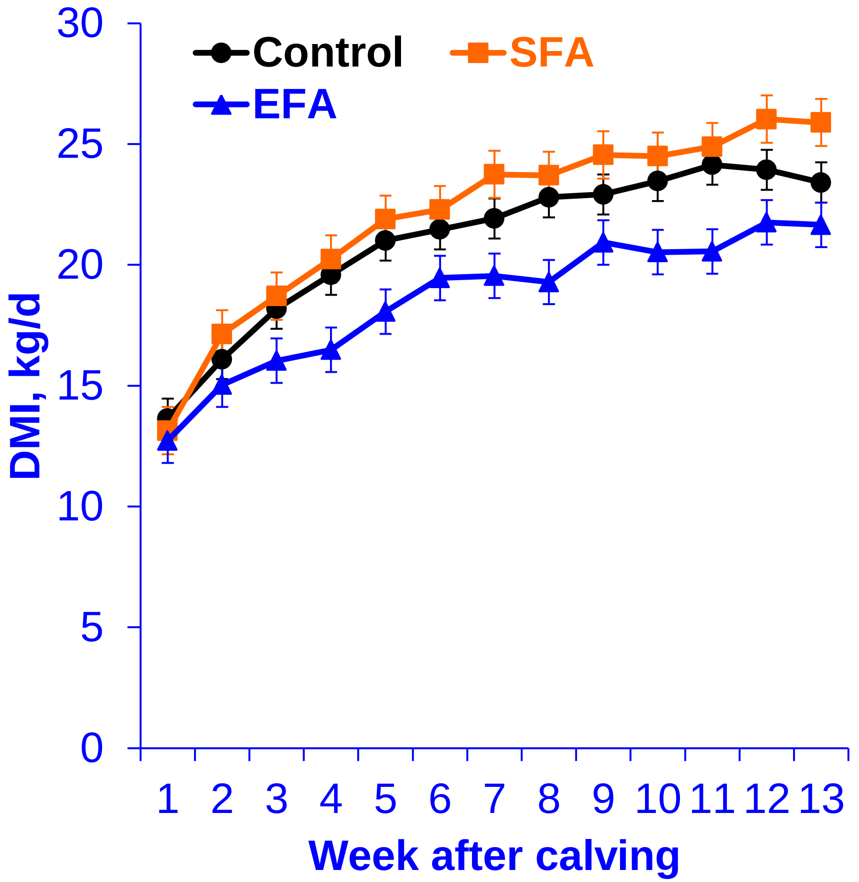
Dietary C18:2: Assigned biohydrogenation of 75% and gut absorption of 80%

Dry matter intake of primiparous and multiparous lactating Holstein cows receiving no fat supplementation (Control), saturated free fatty acids (SFA), or Ca salts of essential fatty acids (EFA)

Primiparous

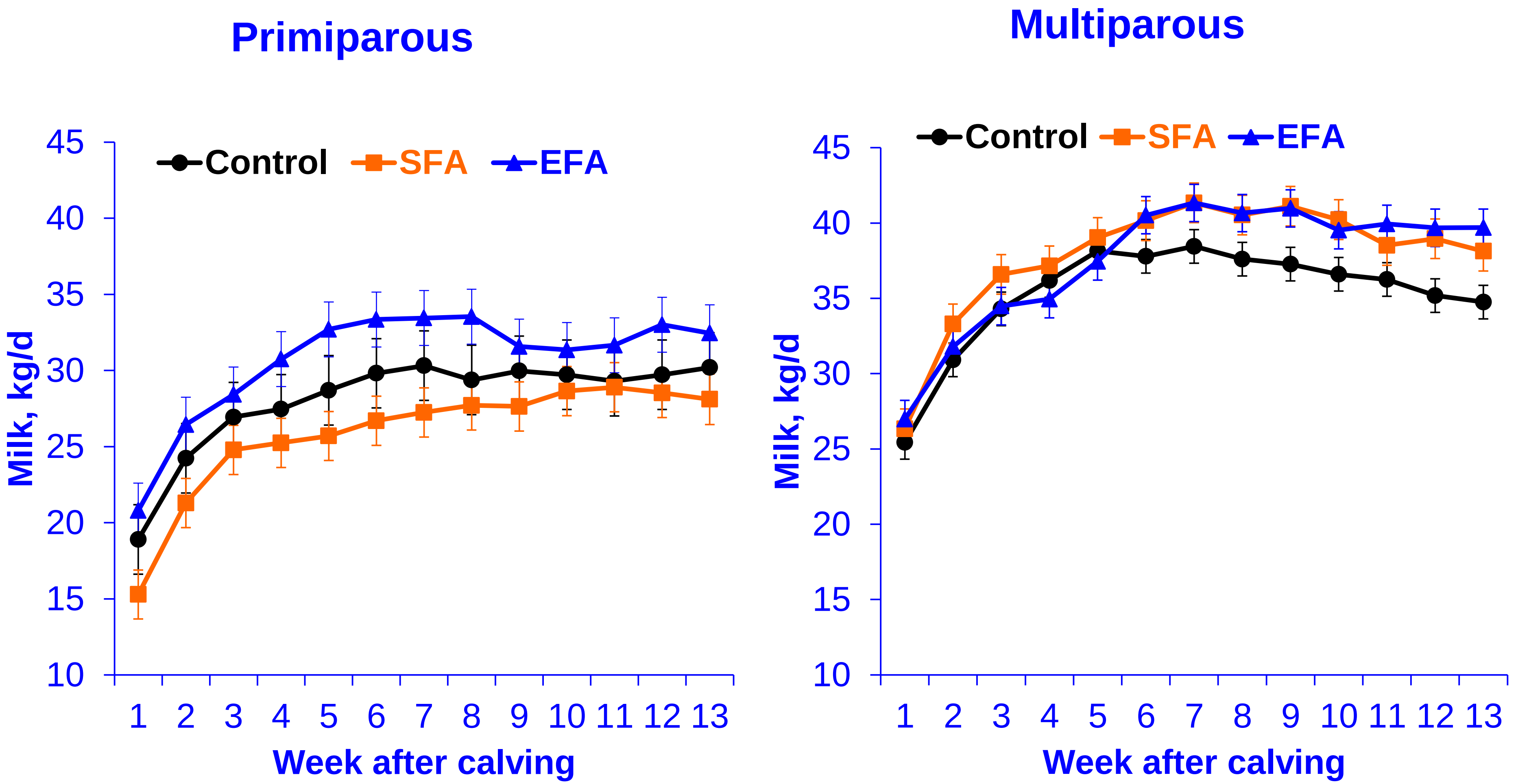


Multiparous



Greco et al. (2010) J. Dairy Sci. 93 (E-Suppl. 1): 448 (Abstr

Milk production of primiparous and multiparous lactating Holstein cows receiving no fat supplementation (Control), saturated free fatty acids (SFA), or Ca salts of essential fatty acids (EFA)



Greco et al. (2010) J. Dairy Sci. 93 (E-Suppl. 1): 448 (Abstr

Fat Supplementation and Hepatic Gene Expression

- Pathways **up regulated** by Fat feedi
  - ✓ Lipid metabolic processes

- Pathways related to lipid metabolism **up regulated** by EFA:
  - ✓ Cholesterol/sterol esterification
  - ✓ Plasma lipoprotein particle assembly
  - ✓ VLDL particle remodeling
  - ✓ Cholesterol/sterol/lipid transporter activity
  - ✓ Sterol transporter activity

Greco et al. (2012) J. Dairy Sci. 95(Suppl. 2):103 (Abstr.).

Materials and Methods

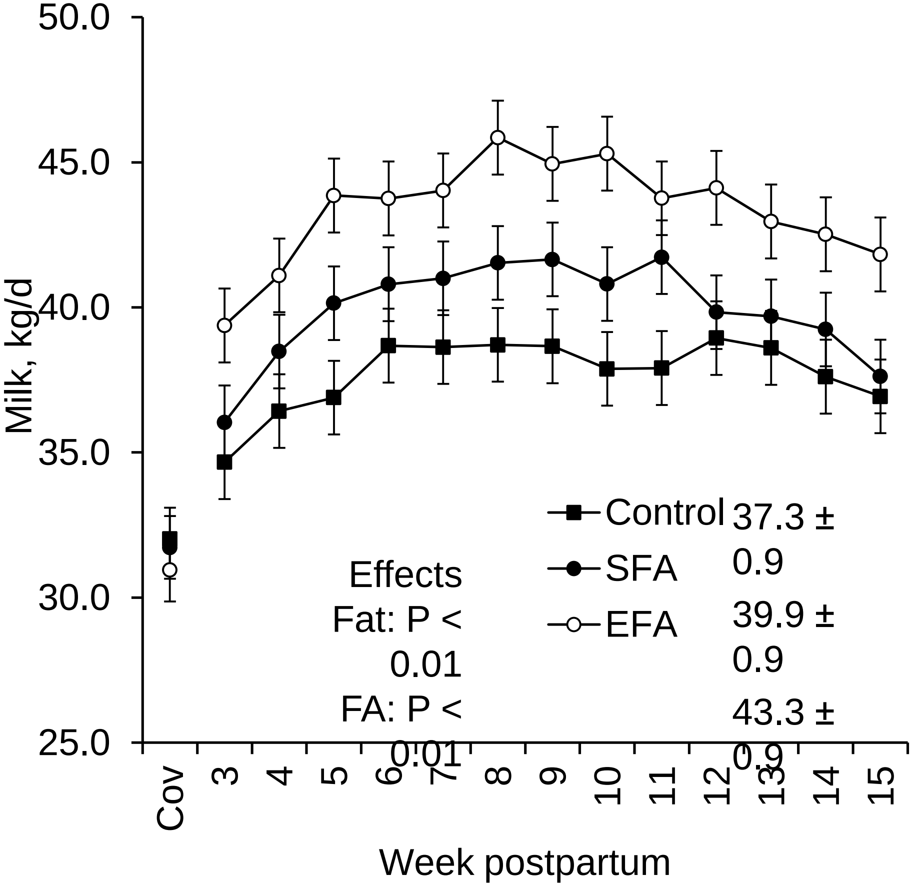
- Cows assigned at 15 DIM to 1 of 3 treatments
  - Control (no fat supplementation)
  - Saturated free FA (SFA, Energy Booster)
  - Ca salts of palm and soybean oils (EFA, Megalac R)

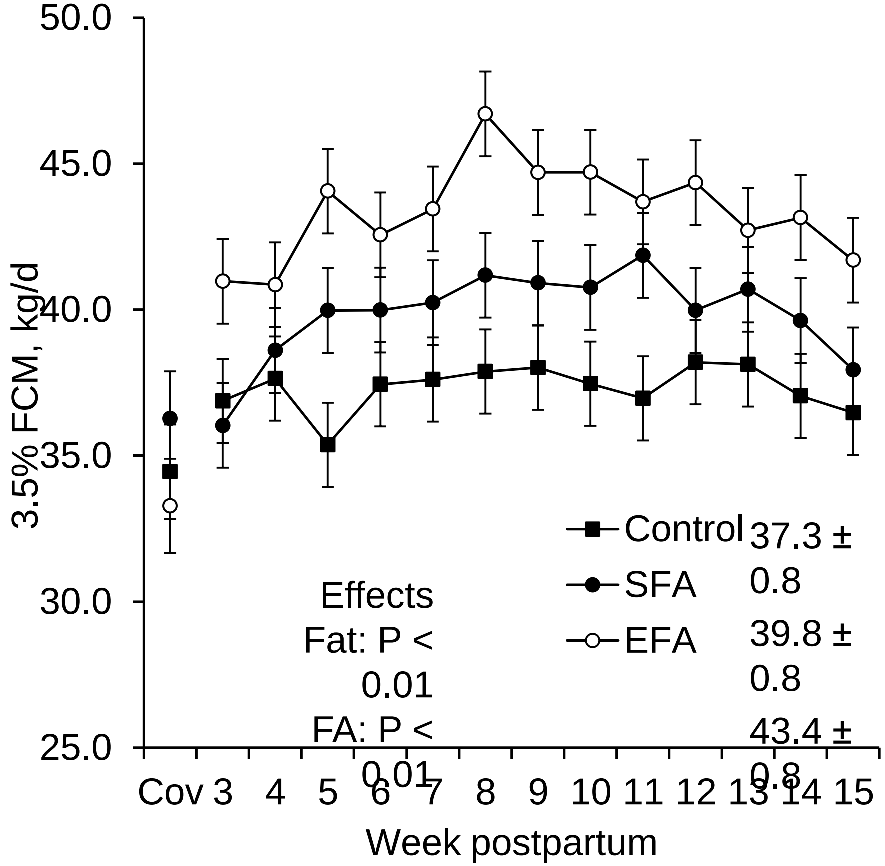
- Control diet was formulated to contain the least amount of essential fatty acids and all diets were high in NDF (37%) with soybean hull replacing corn
  - SFA and EFA replaced corn grain
  - Fatty acids in the diet increased from 2.16 to 3.62%

- Lactation performance was evaluated from day 15 to 106 postpartum (13 weeks)

- Day 15 conceptuses and endometrial tissue were collected twice from each cow for microarray and RT-PCR analyses

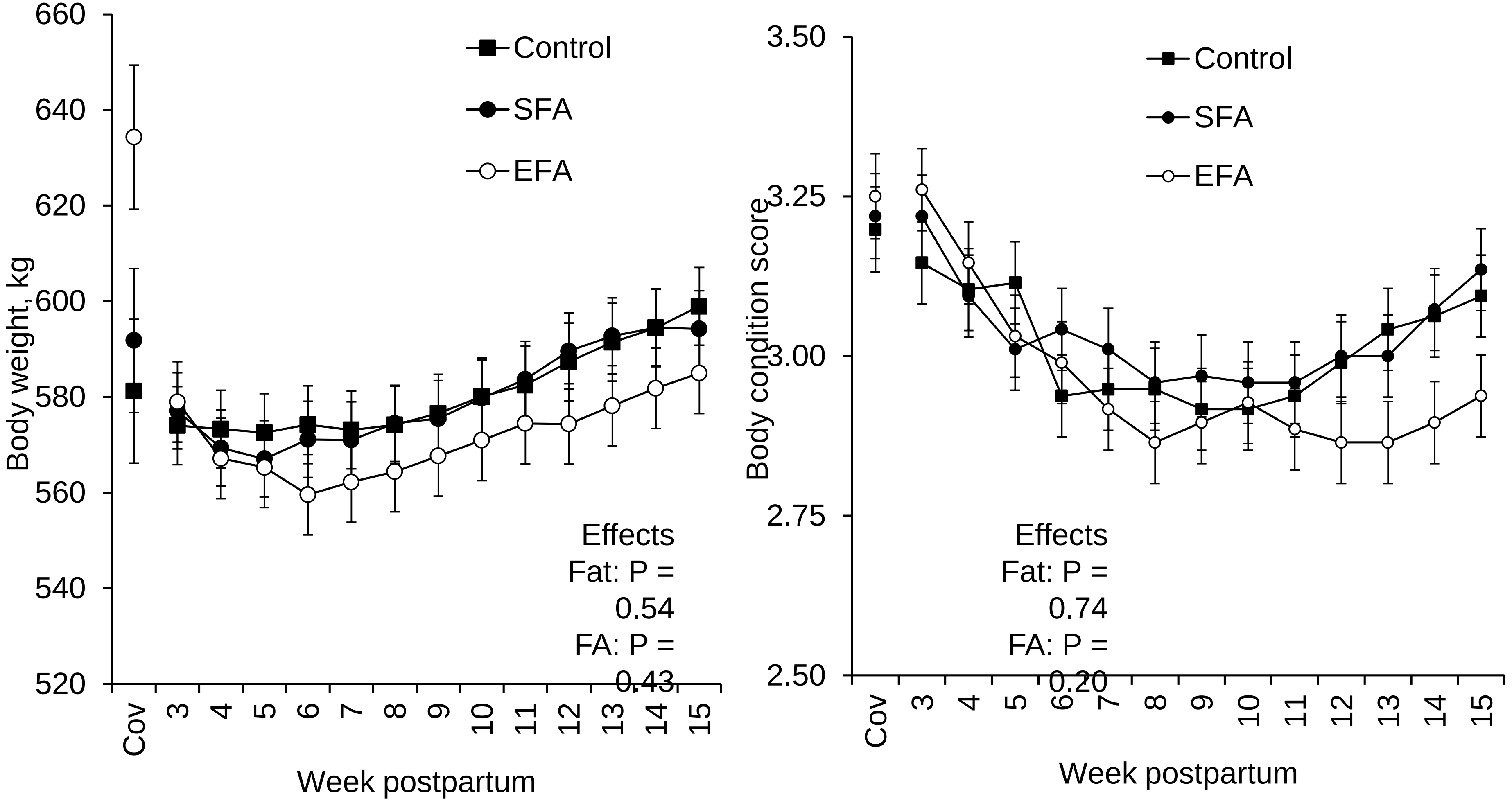
Effect of Fat Sources Differing in FA Profile on Yields of Milk and 3.5% FCM of Early Lactation Dairy Cows





Greco et al. (2011) J. Dairy Sci. 93 (E-Suppl. 1): 448 (Abstr

Effect of Fat Sources Differing in FA Profile on Body Weight of Early Lactation Dairy Cows



Greco et al. (2011) J. Dairy Sci. 93 (E-Suppl. 1): 448 (Abstr

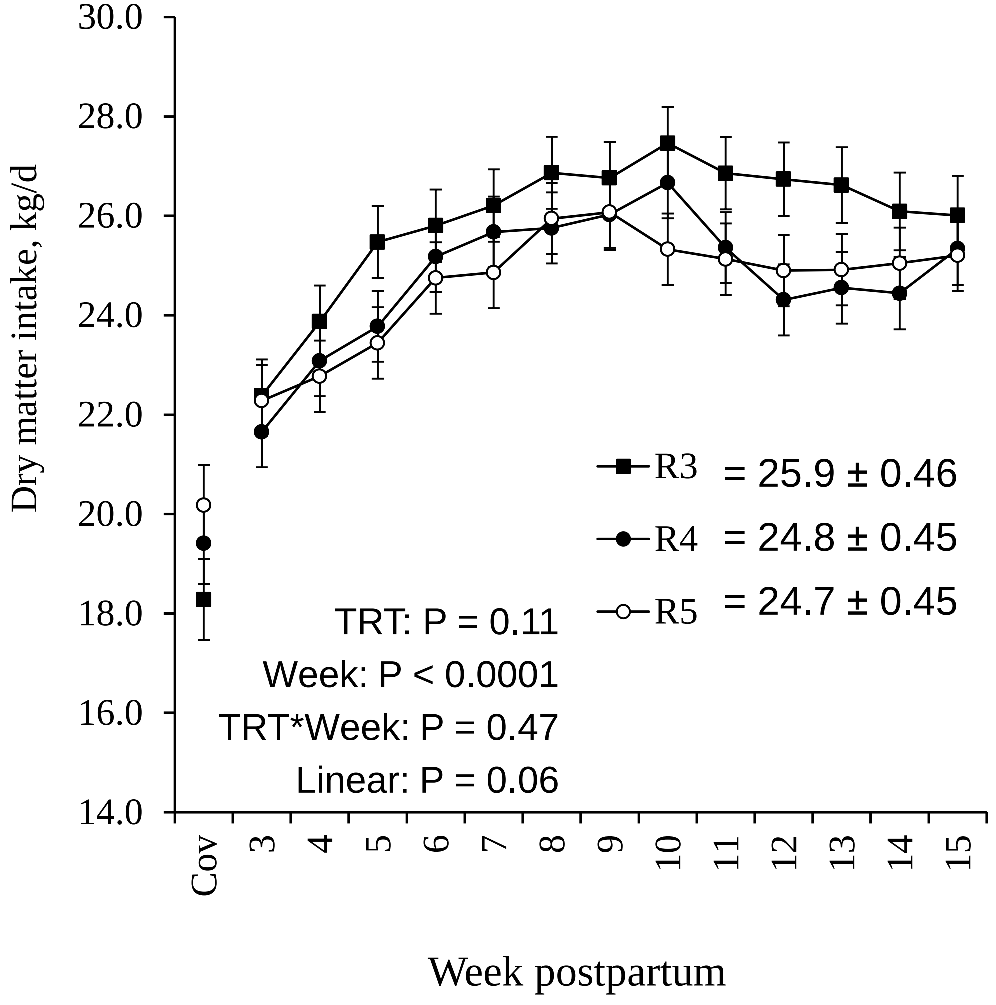
Materials and Methods

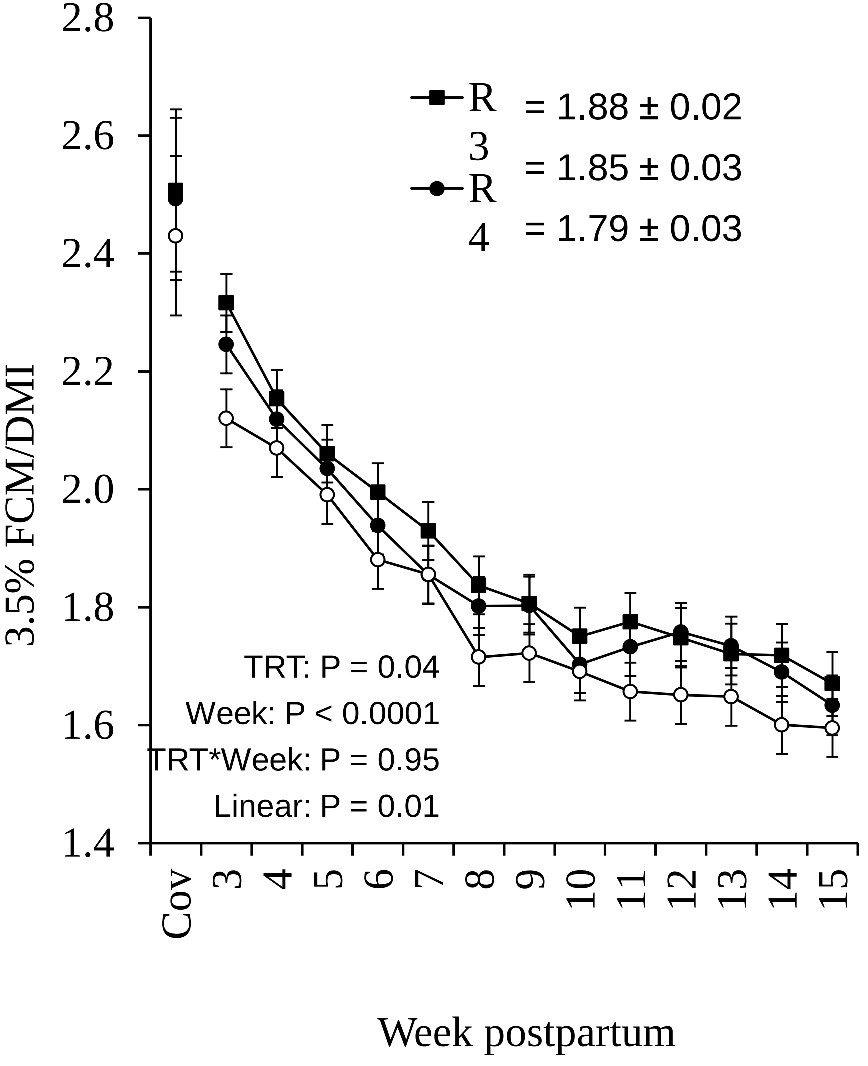
- Multiparous cows assigned to 1 of 3 treatments at 14 DIM

  - TMR with a ratio of n3:n6 FA of 3:1
  - TMR with a ratio of n3:n6 FA of 4:1
  - TMR with a ratio of n3:n6 FA of 5:1

- The FA profile of diets was altered by incorporating Ca salts of fish oil (StrataG), safflower oil (Prequel) and palm oil (EnerGII)
  - All diets contained 38% NDF (soybean hulls) and 3.30% fatty acids

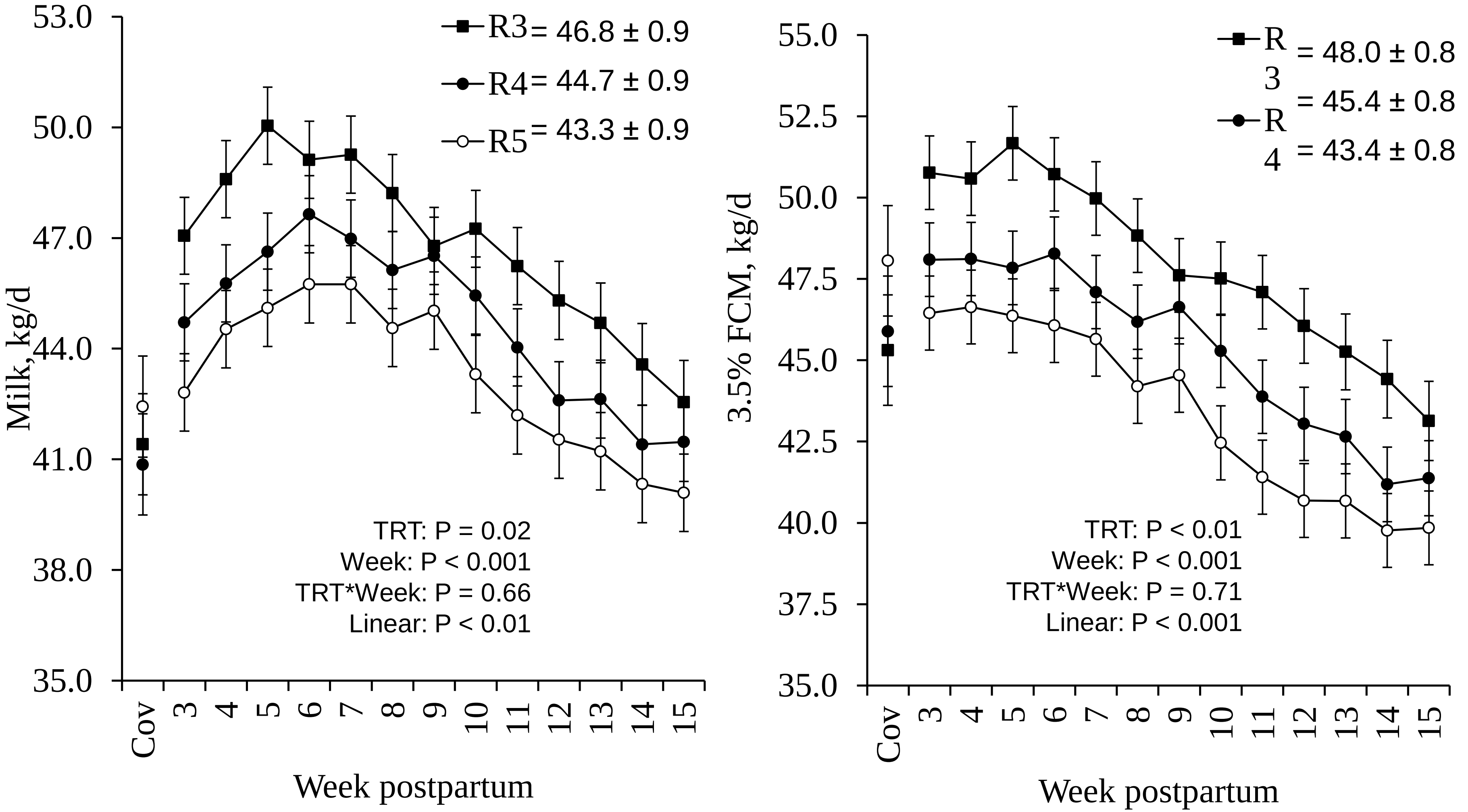
DM Intake and Feed Efficiency of Early Lactation Dairy Cows Fed Diets Containing Different Ratios of n6:n3 Fatty Acids





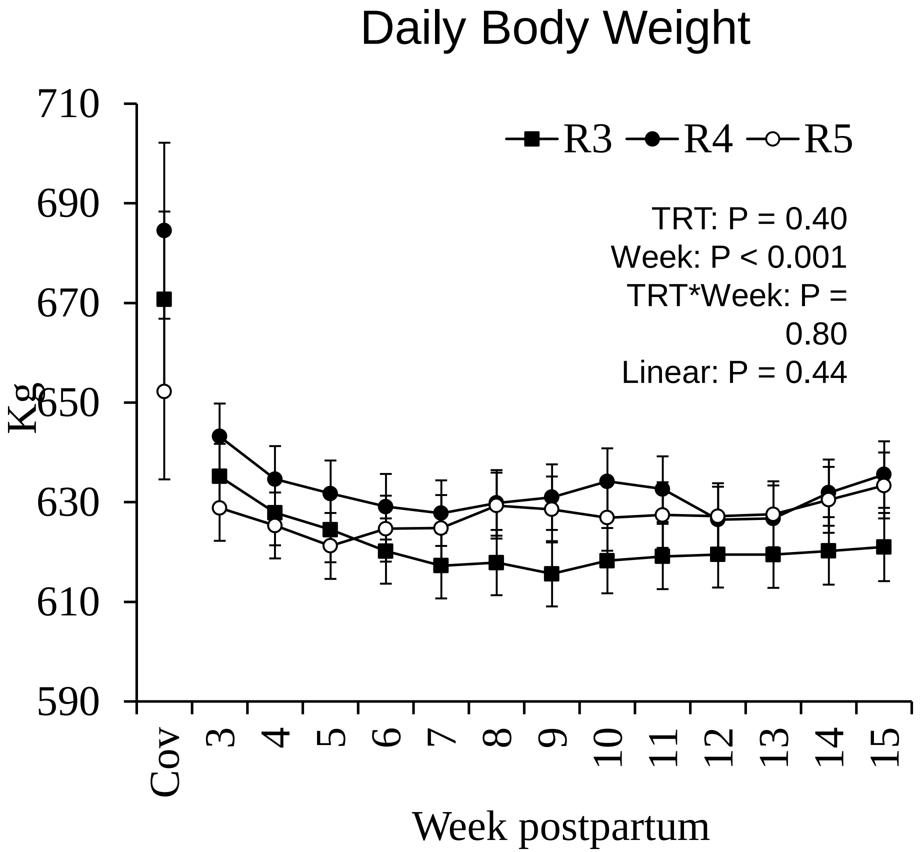
Greco et al. (unpublished results)

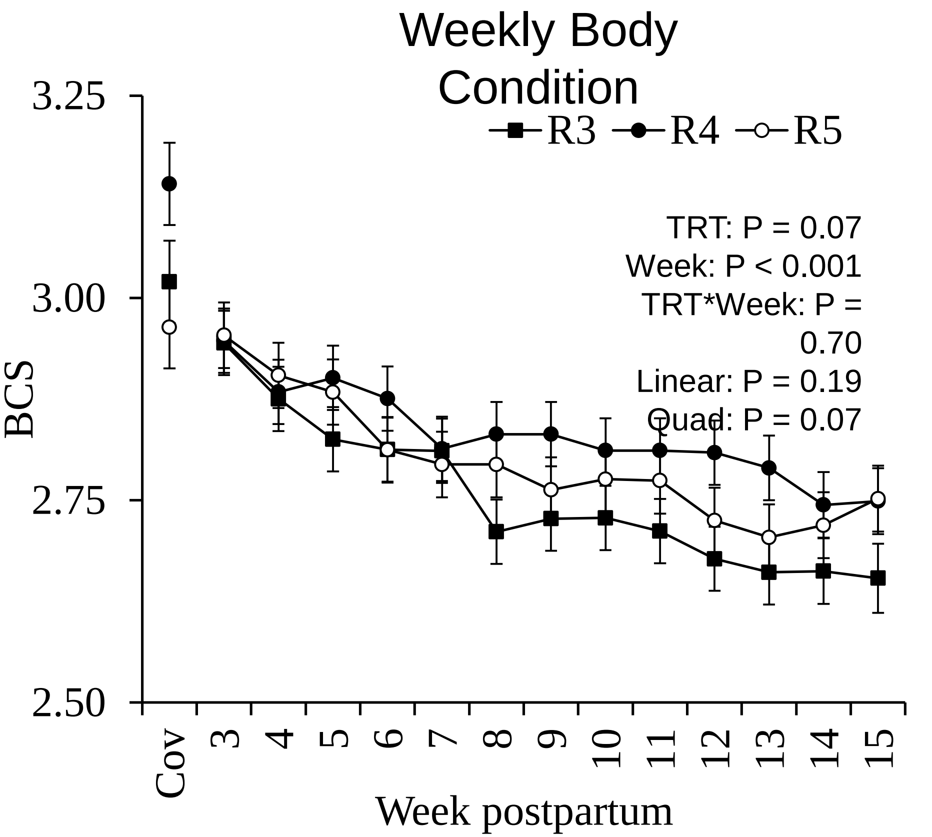
Yields of Milk and 3.5% FCM of Early Lactation Dairy Cows Fed Diets Containing Different Ratios of n6:n3 Fatty Acids



Greco et al. (unpublished)

Body Weight and BCS of Early Lactation Dairy Cows Fed Diets Containing Different Ratios of n6:n3 Fatty Acids

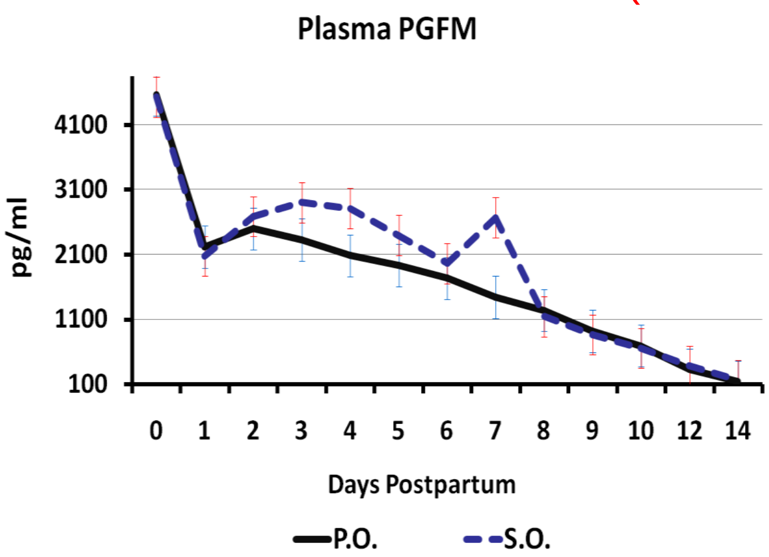


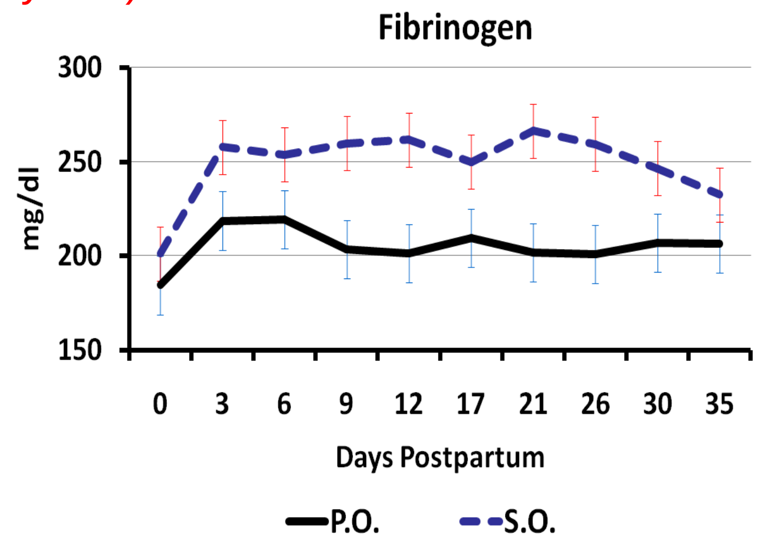


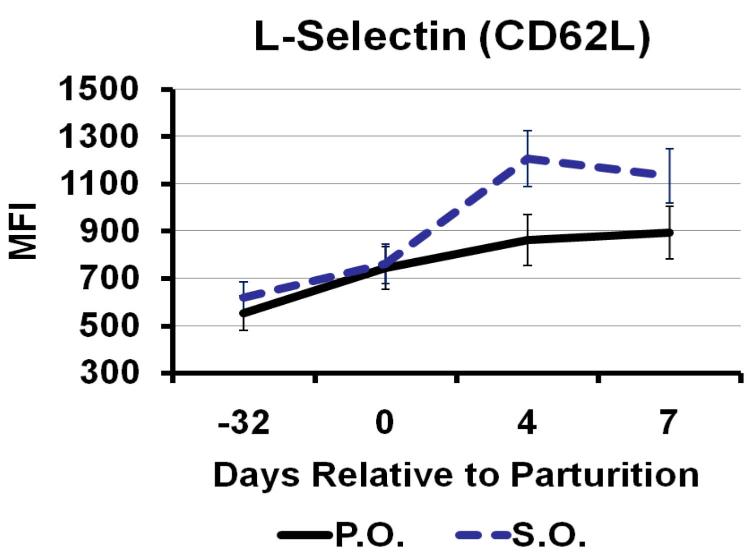
Greco et al. (unpublished results)

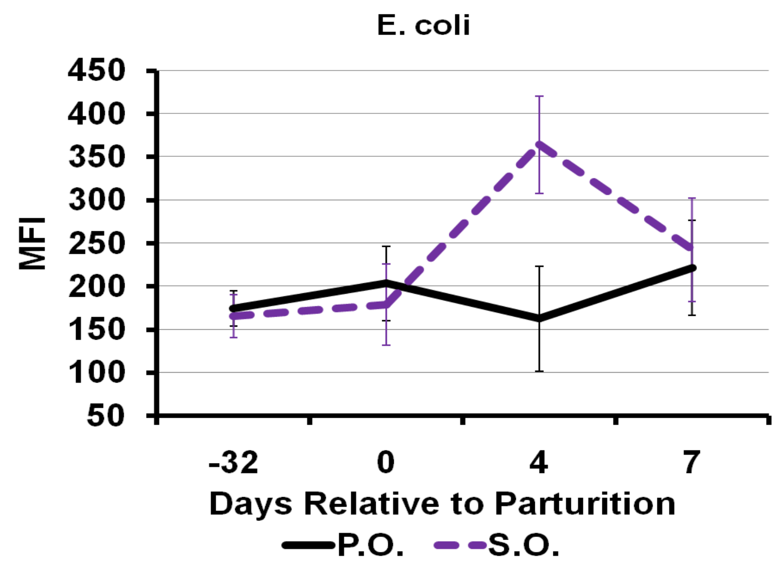
Immune Responses to Differential FA Feeding Ca Salts of Palm Oil vs. Safflower Oil

(Silvestre et al. 2011 J. Dairy Sci.)



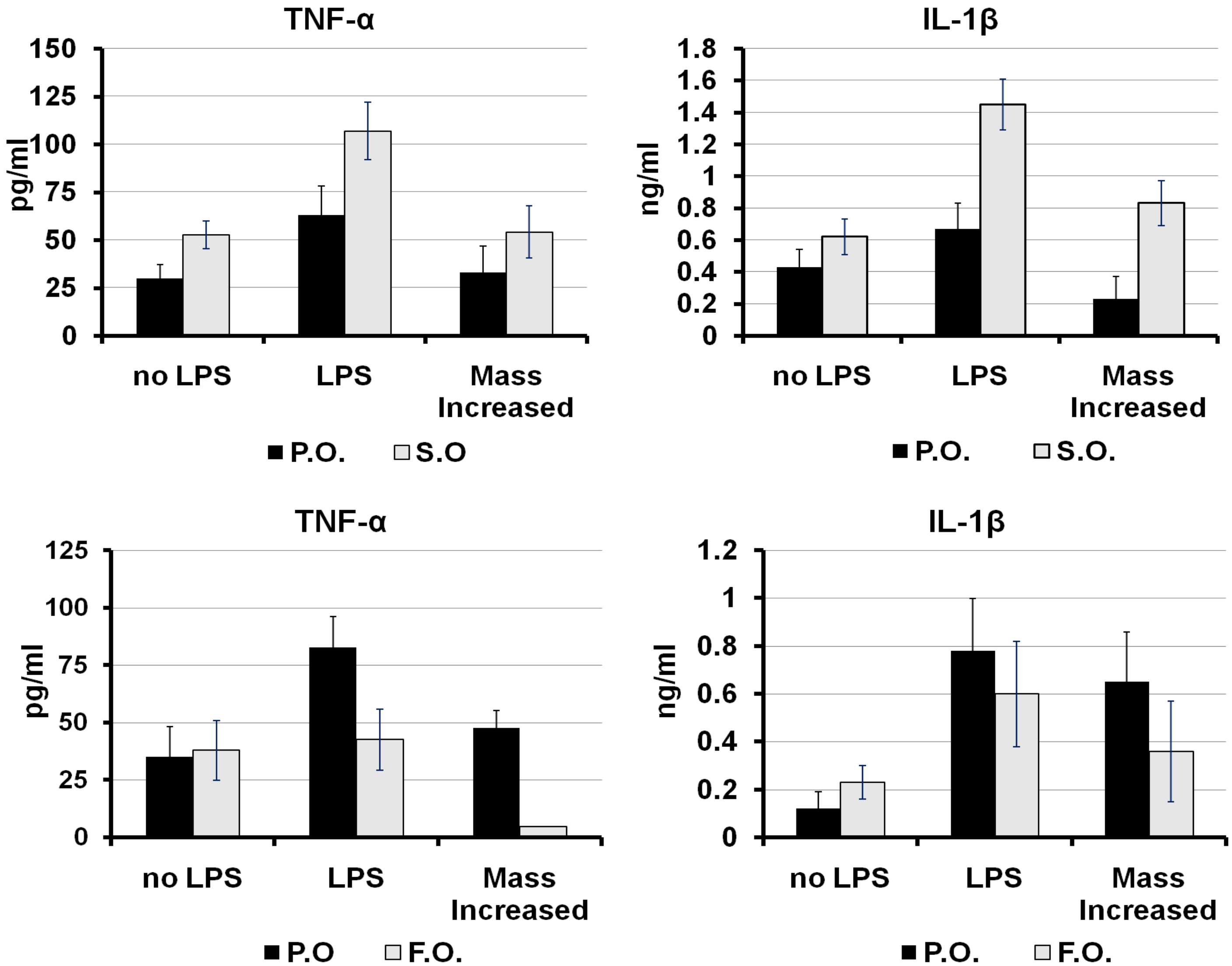






Immune Responses to Differential FA Feeding Ca Salts of Palm Oil vs. Fish Oil

(Silvestre et al., 2011, J. Dairy Sci.)



Uterine Health of Dairy Cows Fed Diets Differing in FA Profile Prepartum

	C18:2 n6 in Supplemental Fat			
	Low	High	P	Reference
	% (number of cows)			
Retained placenta				
	6.5 (246)	6.7 (255)	0.96	Juchem et al. (2008)
	9.8 (579)	10.4 (588)	NS	Silvestre et al. (2011)
Metritis				
	22.3 (246)	24.4 (255)	0.68	Juchem et al. (2008)
	16.8 (579)	18.0 (588)	NS	Silvestre et al. (2011)
Puerperal metritis	15.5 (246)	8.8 (255)	0.08	Juchem et al. (2008)
Periparturient problem*	42.9 (35)	8.3 (12)	0.05	Cullens et al. (2004)

*Includes retained placenta, metritis and mastitis

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Effect of fat source differing in fatty acid profile on metabolic parameters, fertilization, and embryo quality in high-producing dairy cows

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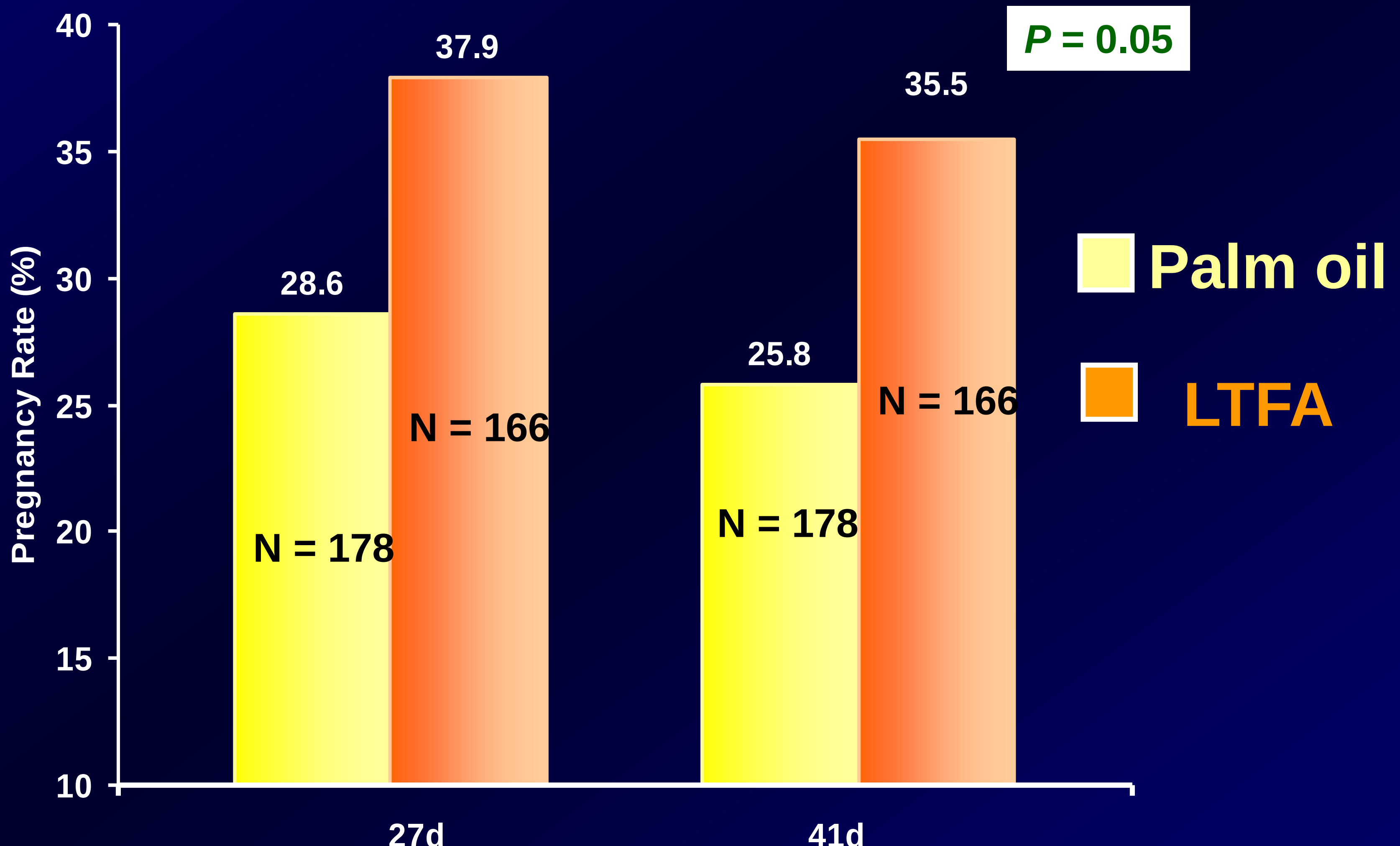
Table 4. Effect of source of dietary fatty acids on recovery, fertilization, and quality responses of embryos-oocytes

	Treatment,[1] % (n/n)				
Item	PO	LTFA	AOR[2]	95% CI[3]	*P*-value
Recovery	59.2 (45/76)	50.0 (39/78)	0.7	0.3–1.3	0.24
Embryo-oocyte					
Fertilization	73.3 (33/45)	87.2 (34/39)	2.5	0.9–7.8	0.10
Grades 1 and 2	37.8 (17/45)	64.1 (25/39)	3.2	1.2–8.3	0.02
Degenerated	15.6 (7/45)	12.8 (5/39)	0.9	0.2–3.3	0.52
Degenerated, unfertilized	42.2 (19/45)	25.6 (10/39)	0.4	0.1–1.1	0.10
Embryos					
Grades 1 and 2	51.5 (17/33)	73.5 (25/34)	3.1	1.0–9.2	0.05
Degenerated	21.2 (7/33)	14.7 (5/34)	1.6	0.4–5.5	0.85
Blastomeres					
Mean ± SEM	19.4 ± 0.7	22.0 ± 0.7	—	—	0.01
Median, n	19	21	—	—	0.23
Live, %	86.9 ± 4.2	95.3 ± 4.2	—	—	0.15
Acessory spermatozoa, n					
Mean ± SEM	21.1	33.3	—	—	0.001
Median	8.0	15.0	—	—	0.19
Embryo-oocyte ≥1	82.2 (37/45)	89.7 (35/39)	1.9	0.5–6.8	0.33

[1]PO = calcium salt of palm oil; LTFA = calcium salt of linoleic and *trans*-octadecenoic acids.
[2]AOR = adjusted odds ratio. The PO treatment was used as the referent group.
[3]CI = confidence interval.

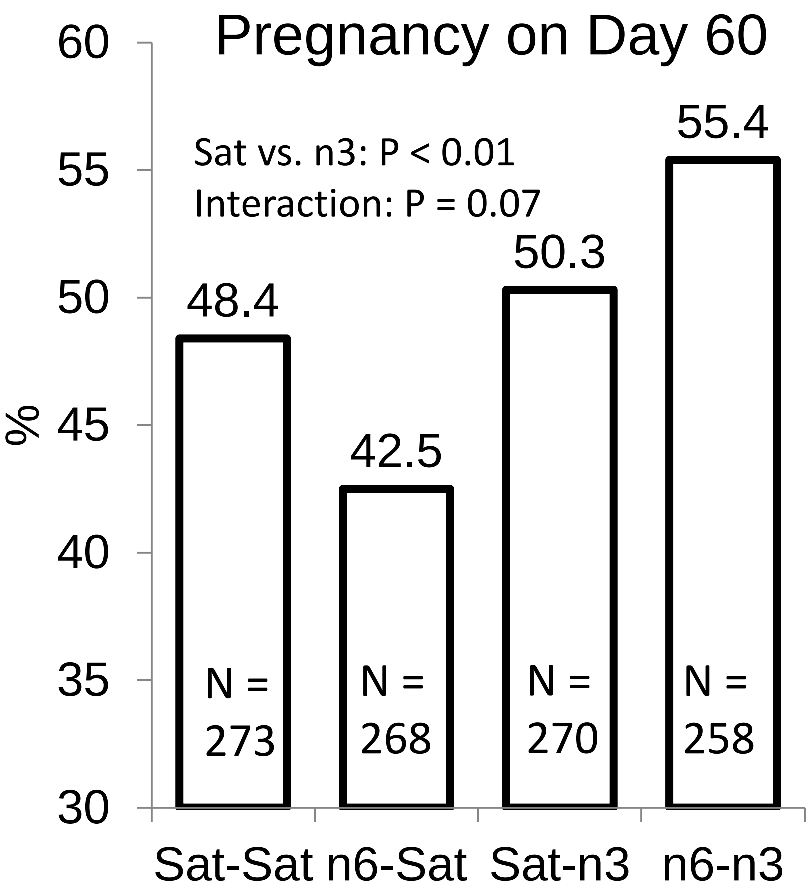
Source of Fatty Acids and Pregnancy at 1st Postpartum AI

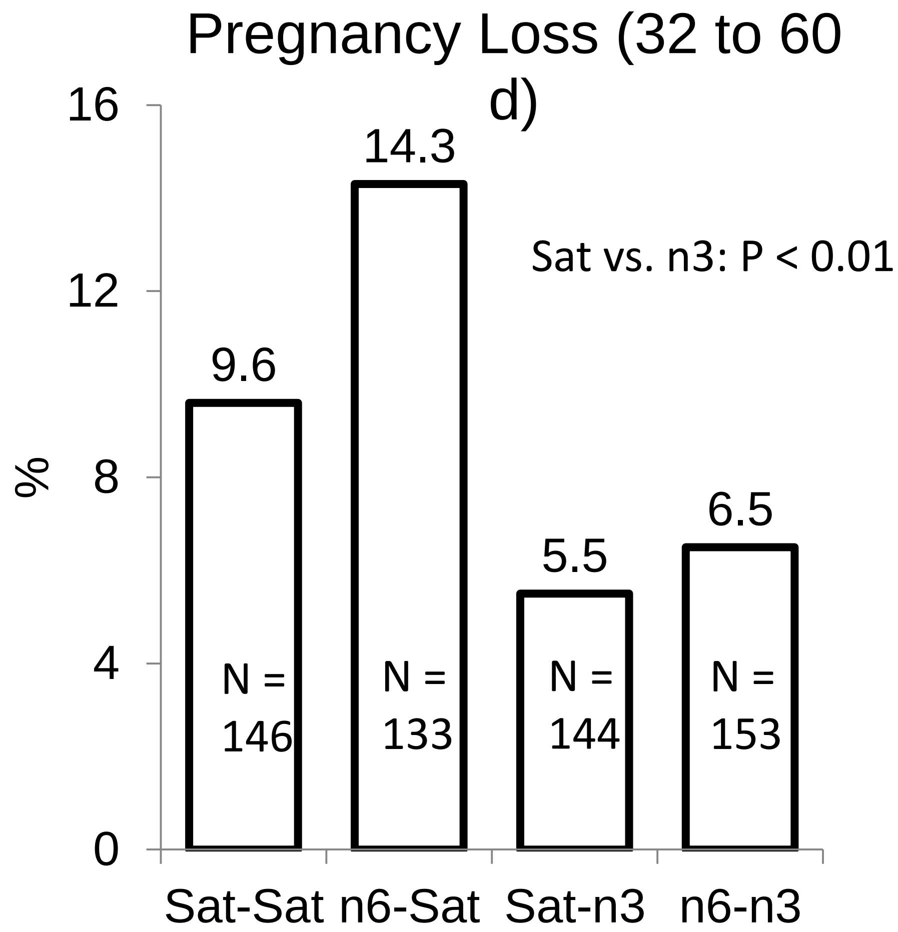


Juchem *et al. Reprod. Dom. Anim.* (2008)

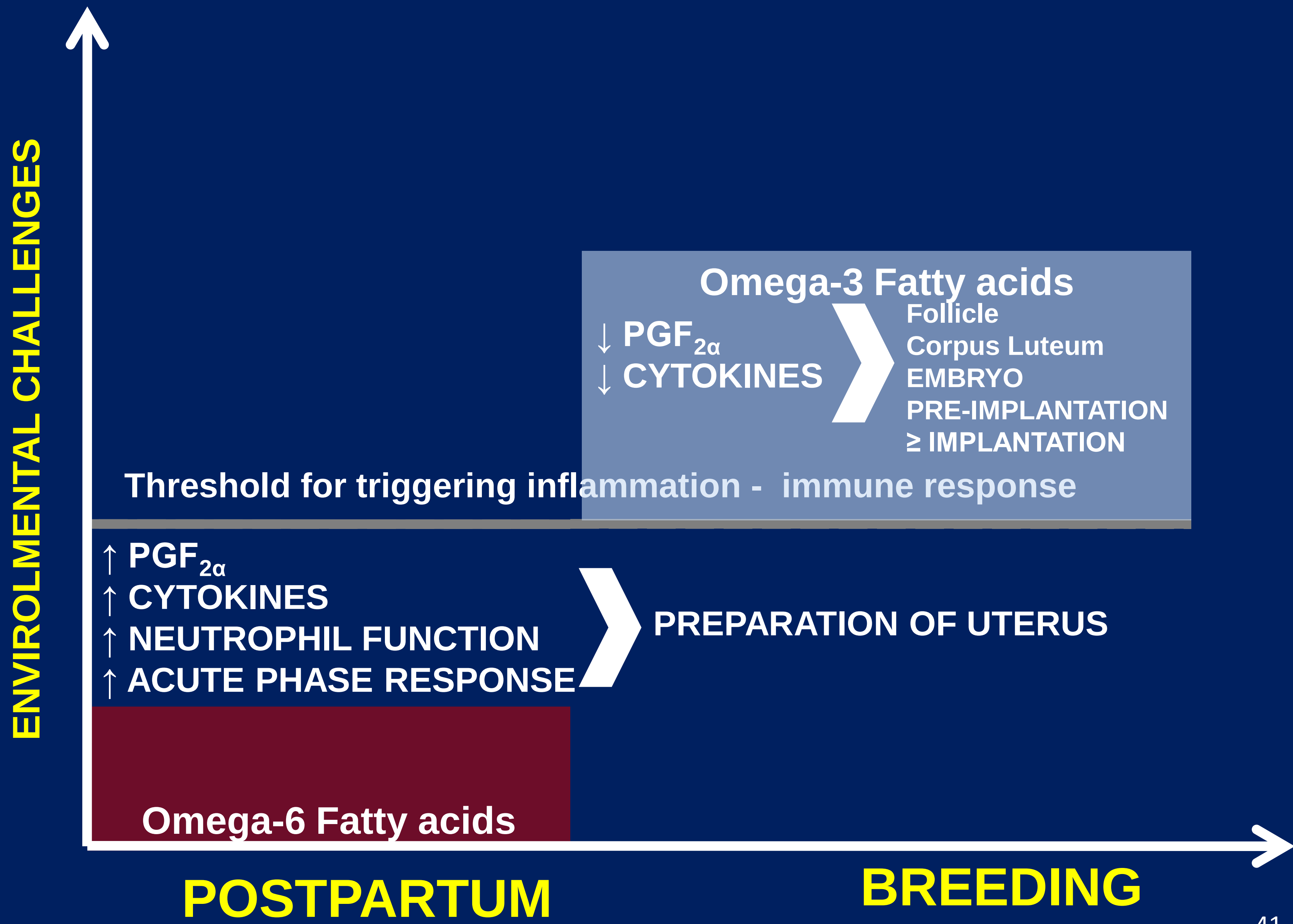
Effects of Fatty Acid Supplementation During the Transition and Breeding Periods on Fertility of Dairy Cows

Transition diets = -30 to 30 DIM
Breeding diets = 30 to 160 DIM





Silvestre *et al.* (2011) J. Dairy Sci. 94 :189–204



Silvestre *et al.* (2011) J. Dairy Sci. 94 :189–204

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