VEERkracht
Veterinaire Kenniscoöperatie voor de Melkveehouderij U.A.

Healthy cows, fertile cows?

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31-01-2019

Fertility need a multifactorial approach…

"Infertility problems in dairy cattle are multifactorial and are associated with both genetics and management.

Individual cow factors relating to the age and health of the animals, the amount of feed consumed and how it is utilized internally (nutrient partitioning) influence their ability to **conceive** and **remain pregnant**."

Wathes (2012)

Fertility need a multifactorial approach…

To breed
- Fast resumption of regular estrus cycling

To concieve
- High oocyte quality → Prof Leroy
- Uterine environment
  - Support conception
  - Support elongation of the embryo
  - Promote materal/foetal crosstalk

To remain
- High progesterone

Uterine disease

- Endometritis
  - -16% preg rate (Fourichon, 2000)
  - -31% RR preg 150 days (Fourichon, 2000)
  - 118 days open (mean) vs 208 days (Gilbert, 2005)
  - Cytological endometritis → OR 0,65 preg after 1^{e} ins (Lee, 2018)

- 0-14 days pp. positive endometrial cultures usually include:

One or more from Trueperella Pyogenes	E. coli
Streptococcus spp.	Pasteurella Multocida
Staphylococcus spp.	Pseudomonas spp.
Clostridium spp.	Fusobacterium spp.
	Bacteroides spp.

(LeBlanc, 2008;Chapwanya et al., 2012).

- The cells of the endometrium express the specific receptor complex for detection of LPS, and LPS switches prostaglandin secretion from $F_{2\alpha}$ to E_2, which likely disrupts luteolysis (Dobson, 2007)

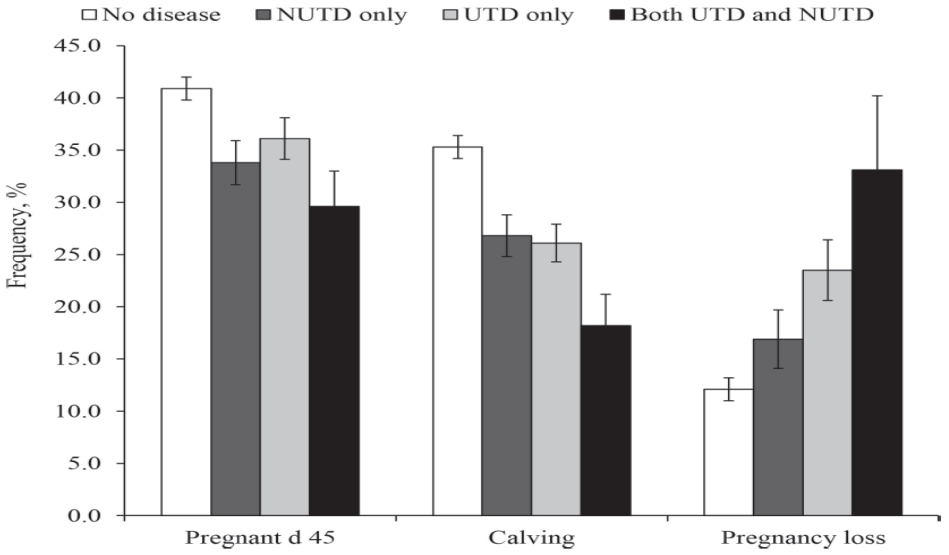
Oocyte quality and/or disease?

Item	Adjusted mean ± SEM [1]			
	No disease-AI	Disease-AI	No disease-ET	Disease-ET
Pregnant day 45	38.8 ± 1.8	31.0 ± 2.1	40.7 ± 1.7	35.9 ± 2.4
Calving	32.9 ± 1.7	22.2 ± 1.9	35.9 ± 1.7	28.2 ± 2.2
Pregnancy loss	12.4 ± 1.5	21.3 ± 3.1	11.1 ± 1.5	22.4 ± 3.4

n=4206 cows
n(AI)=?
n(ET)=?

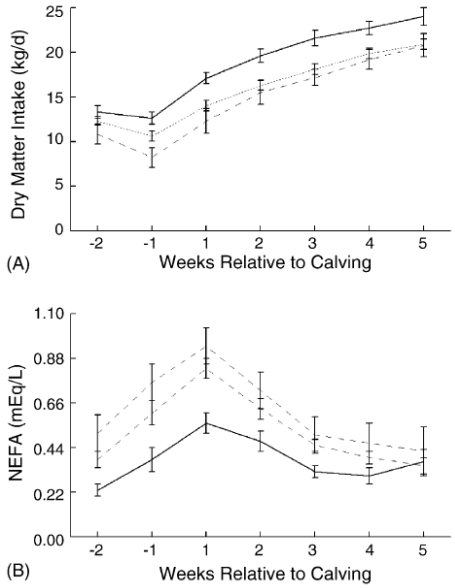
Ribiero and Carvalho (2017) Anim. Repr. 14 P589-600

Does source matter?



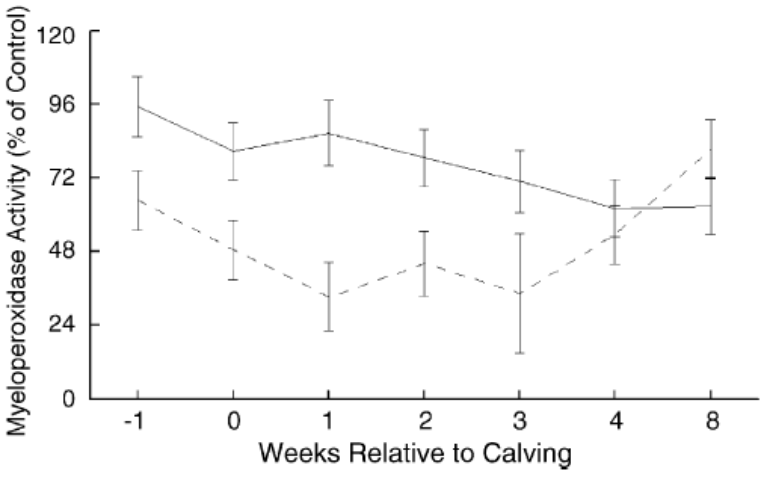
Ribiero et al (2016) JDS 99 P2201-2220

Transition is key to success



Hammon et al. (2006) Vet. Imm and Imm. 113 P21-29

Transition is key to success



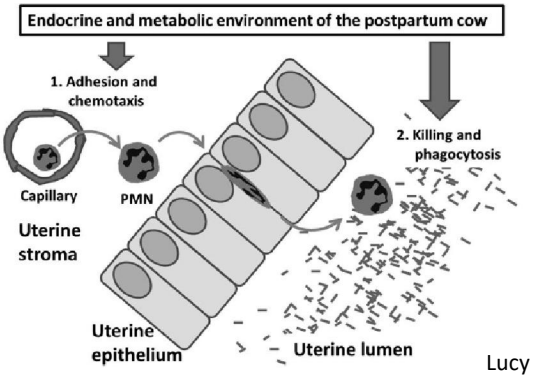
Hammon et al. (2006) Vet. Imm and Imm. 113 P21-29

Transition is key to success

Table 1 *Hormones and metabolites affected by milk production in* postpartum *dairy cows, their known effects on polymorphonuclear neutrophil (PMN) function, and relative concentrations (*postpartum v. *later lactation)*

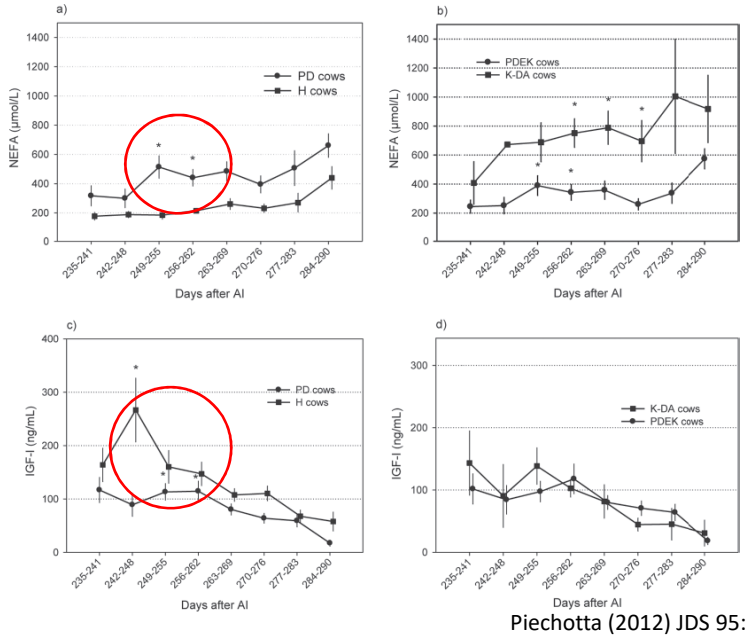
Item	Known effects on PMN function (reference)	*Postpartum*
Insulin	Activates growth factor pathways; ↑ cytokine production; ↑ chemotaxis; ↑ phagocytic activity (Sunahara *et al.*, 2012)	Low insulin
IGF1	Cell-survival factor; activation of PI3K (Himpe *et al.*, 2013)	Low IGF1
Glucose	↑ respiratory burst; ↑ chemotaxis; ↑ phagocytosis (Chou *et al.*, 2010)	Low glucose
BHBA	Inhibits formation of extracellular traps and inhibits bactericidal activity against *Escherichia coli* (Grinberg *et al.*, 2008)	High BHBA
NEFA	↓ production of reactive oxygen species (Ster *et al.*, 2012)	High NEFA

BHBA = β-hydroxy butyric acid; NEFA = non-esterified fatty acid.



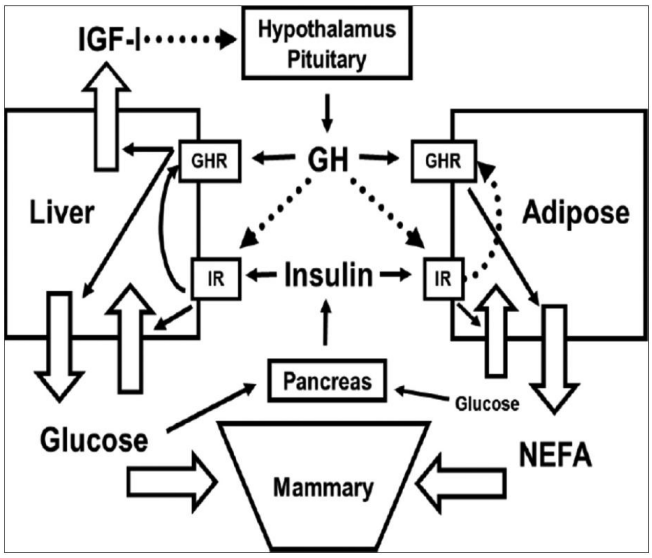
Lucy (2014) Animal 8 P82-90

Is energy prepartum the key?



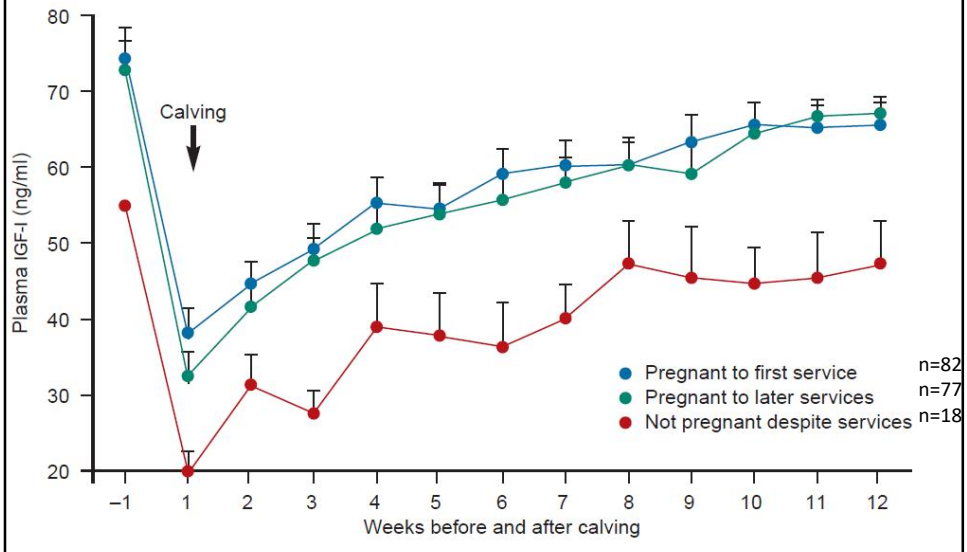
Piechotta (2012) JDS 95: 1367-1370

Short overview HPA



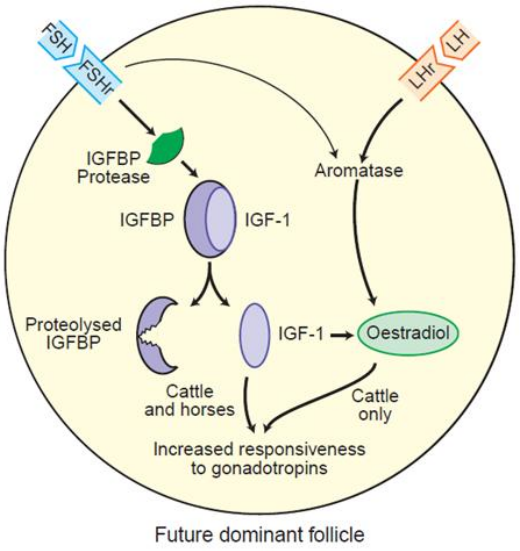
Wankhade et al. (2017) Vet. World 10 P1367-1377

Energy status predictive?



Taylor et al. (2004) Vet. Rec. 155 P583-588)

Energy status predictive?



Beg and Ginther (2006) Reproduction 132 P365-377

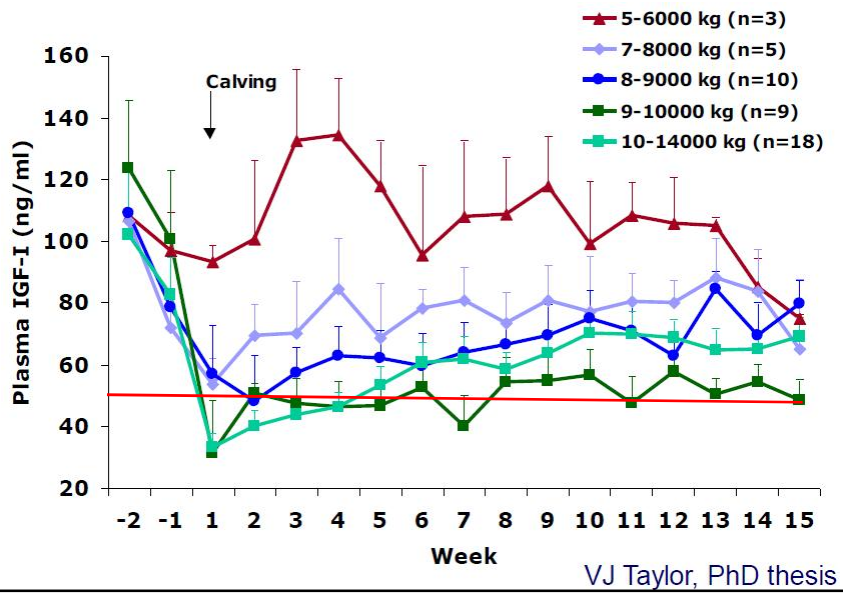
Energy status predictive?

TABLE 5: Suggested diagnostic values of plasma insulin-like growth factor-I (IGF-I) for predicting the fertility of multiparous, high-yielding dairy cows

Prediction	Plasma concentration of IGF-I One week after calving	At first service
Likely to conceive to first service	>25 ng/ml	>50 ng/ml
Unlikely to conceive to first service	<25 ng/ml	<50 ng/ml

Taylor et al. (2004) Vet. Rec. 155 P583-588)

Energy status predictive?



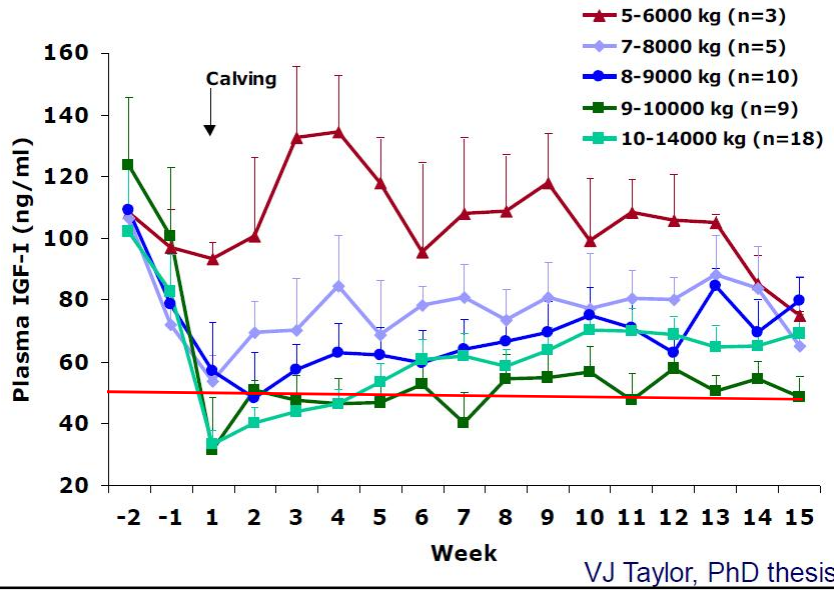
VJ Taylor, PhD thesis

Example:
High production, good repro figures

- 10.220 kg avg, 4.32% Fat, 3.54% Protein, SCC 95
- Replacement (an) 23%
- Peak-yield avg >45 kg/day

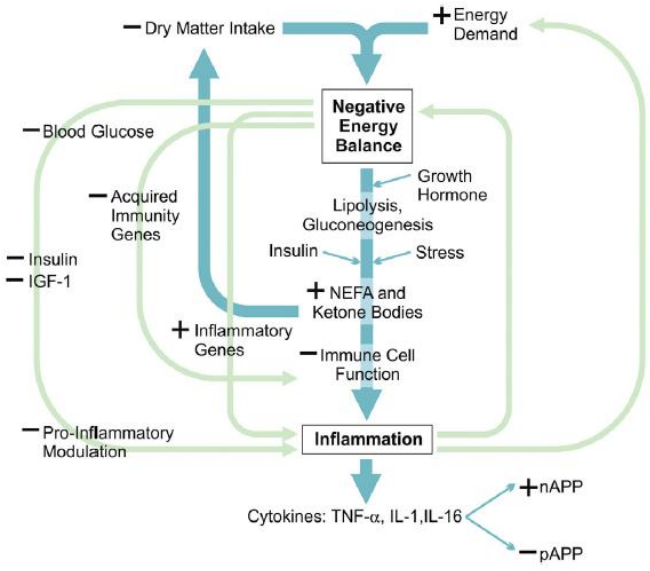
- Calving interval 375 days
- First insemination 75 days pp (avg)
  - VWP 60 days
- Number of inseminations 2.09/inseminated cow

Energy status predictive?



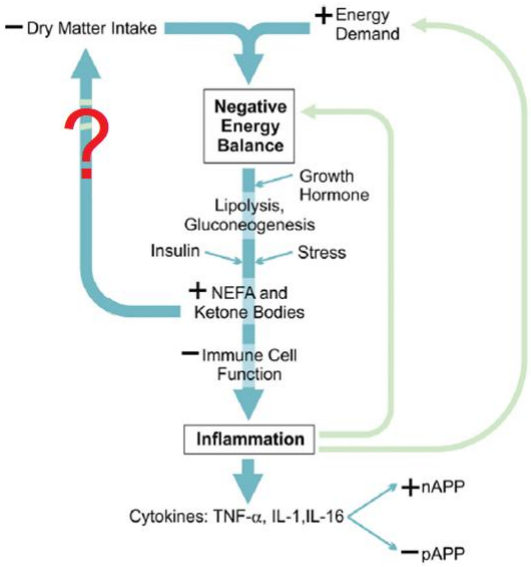
VJ Taylor, PhD thesis

When is NEB a problem?



Esposito et al. (2014) An. Rep. Sci 144 P60-71

NEFA are in question!



NEFA are in question!

- 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?

Baumgard (2017)

Intriguing statements…

- Association and correlation
  - No cause and effect
- Infusing ketones or NEFA does not cause negative outcomes
- Ketones do not decrease feed intake
  - Otherwise a starving animal would not have an appetite
- Infusing ketones do not increase blood ketone levels
  - In late lactation ketone removal from the circulating pool is very rapid
- Cannot recreate ketosis during established lactation
  - Using a feed-restriction model doesn't cause fatty liver and ketosis
- Some females do not consume food after parturition
  - Ocean mammals

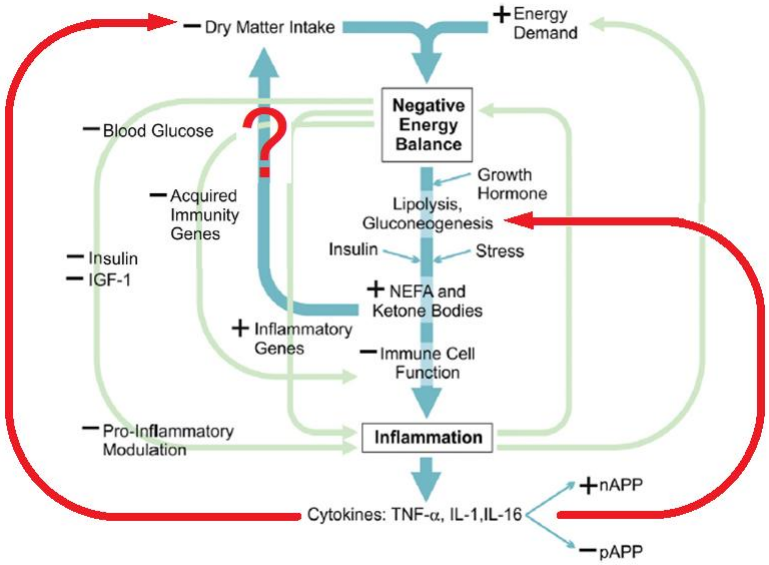
Baumgard (2017)

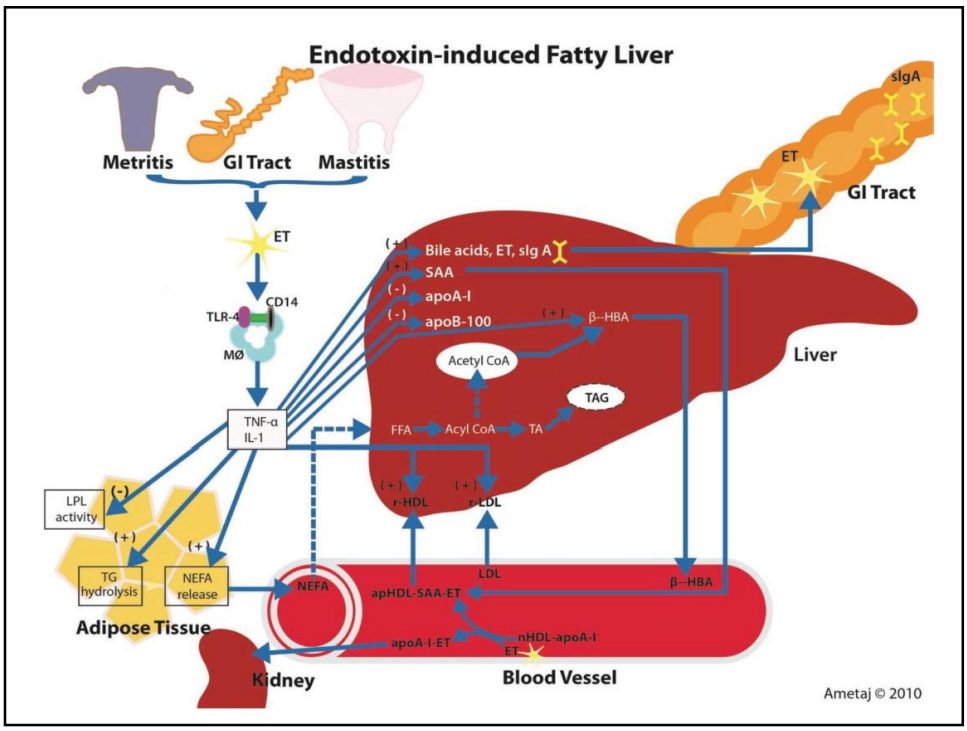
NEFA in human

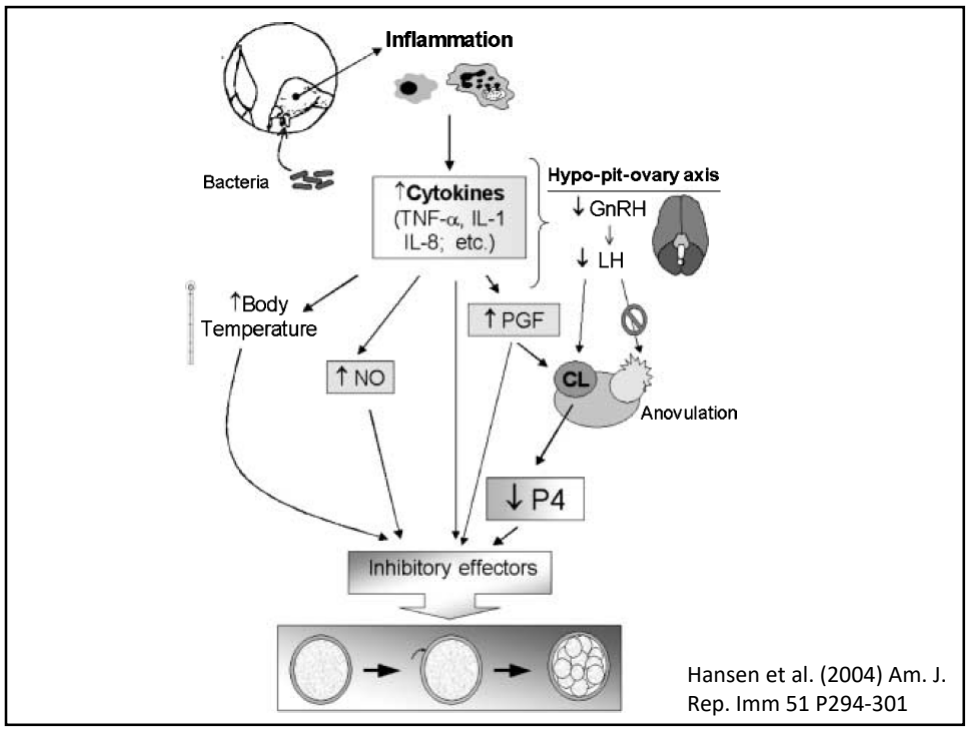
- Inflammation can compromise the liver's ability to export lipid and increases NEFA incorporation into hepatic triglycerides
  - Without high plasma NEFA
  - Acute phase proteins ↑
  - Increased circulating LPS

(Ma et al. 2008)

Think about this morning lectures!







Hansen et al. (2004) Am. J. Rep. Imm 51 P294-301

Maternal recognition

- Endotoxin (LPS) → Inhibit pulsatile LH-secretion (Suzuki, 2001)
- INF-ß → decrease of LH secretion (Mc Cann, 2000)
- TNF-α and INF-δ → cytotoxicity in CL → P4↓
  - Suboptimal Luteal function → Histotroph secretion ↓ → INF-τ → Maternal recognition (Robinson, 2008)

Maternal recognition

- TNF-α and IL-1ß → secretion of $PGF_{2\alpha}$ ↑(Hansen, 2004)
- BUN ↑ → Uterine PH ↓ → secretion of $PGF_{2\alpha}$ ↑ (Tamminga, 2006)

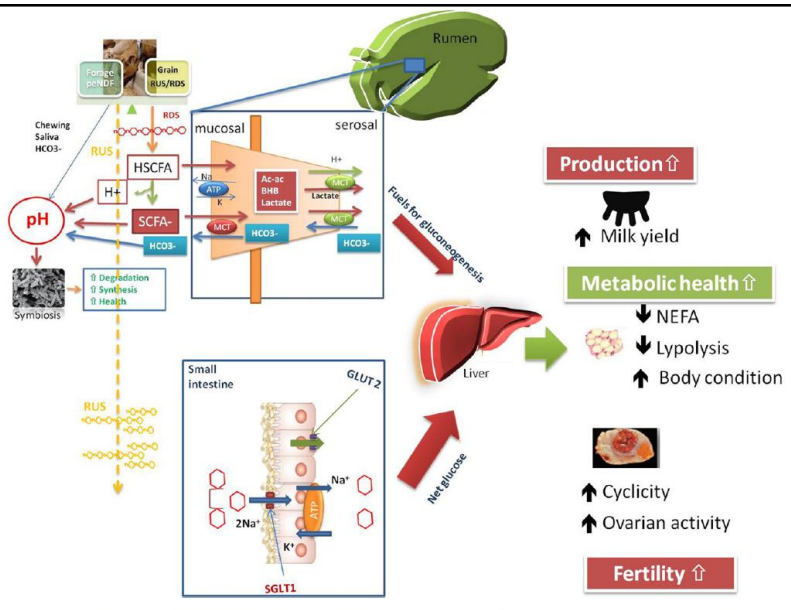


Fig. 1. Graphical presentation indicating the role of balanced nutrition in rumen pH regulation and proper functioning as well as in the contribution to gluconeogenesis and glucose pools with implications in health and fertility in cows: BHB, β-hydroxybutyrate; Ac-ac, acetoacetate; RDS, rumen degradable starch; RUS, rumen undegradable starch; peNDF, physically effective neutral detergent fiber; SCFA, short-chain fatty acids in protonated (HSCFA) or ionic (SCFA-) form; HCO_3^-, bicarbonate, NEFA, non-esterified fatty acids; MCT, monocarboxylate transporters; SGLT-1, sodium coupled glucose transporter 1 and GLUT-2, facilitated glucose transporter 2.

Zebeli et al (2015) Res. Vet. Sci 103 P126-136

SARA and systemische inflammation

	Rumen		Plasma/Serum			
Source (SARA)	PH<5,6 (min/d)	ΔLPS (EU/mL)	ΔLPS (EU/mL)	ΔSAA (µg/mL)	Δ HP (µg/mL)	ΔLBP (µg/mL)
Alfalfa	**268**	**+60,139**	**0**	**-15,3**	**-29**	**-3,8**
Grains	**279**	**+47,579**	**+0,52**	**+269,2**	**+479**	**+34,9**

Khafipour et al (2009 A/B)

Peripheral inflammation

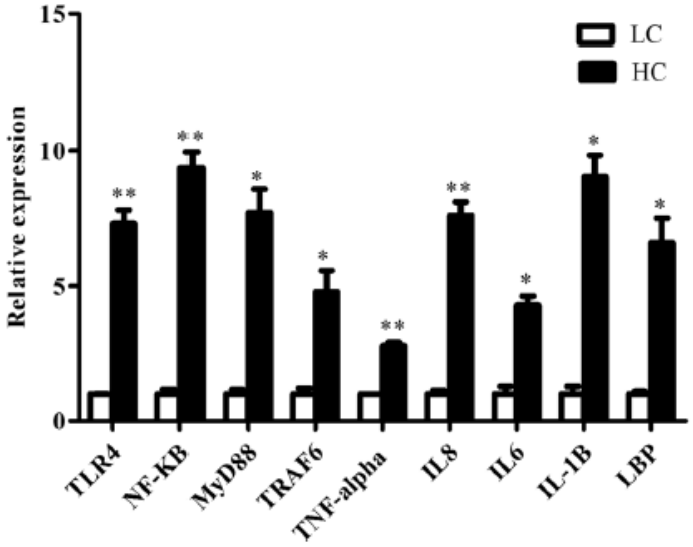
Table 3 LPS concentration in rumen and plasma of dairy cows fed low concentrate (LC) and high concentrate (HC)

LPS concentration (EU/mL)	Treatment[a]			
	LC	HC	SEM[b]	*p*-Value
Rumen LPS	47170	79040	7966.25	<0.01
Jugular vein Plasma LPS	470	860	81.26	<0.001

[a]*HC* high concentrate diet, *LC* low concentrate diet, *EU* endotoxin unit
[b]*SEM* Standard error of the mean between the two groups
The LPS data were compared using Student's *t*-test between HC and LC groups
$P \leq 0.05$ was considered significant

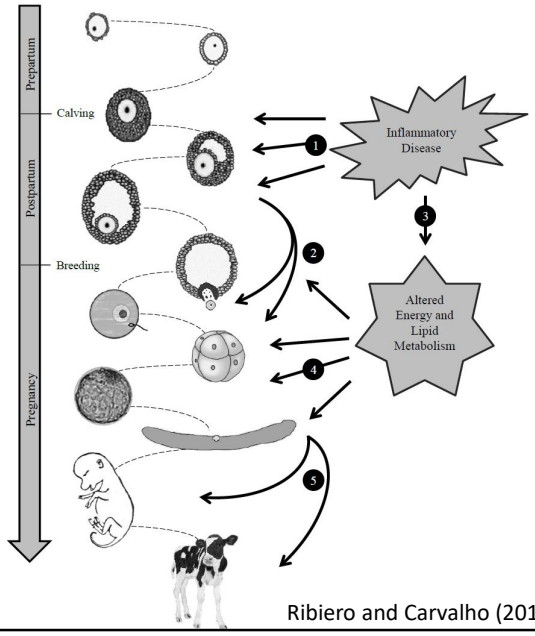
Bilal et al. (2016) BMC Vet. Res. 12 P284-291

Peripheral inflammation



Bilal et al. (2016) BMC Vet. Res. 12 P284-291

Take home …….



Ribiero and Carvalho (2017) Anim. Repr. 14 P589-600