Inflammation, Immune Function, and the Transition Cow

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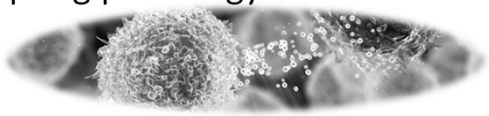
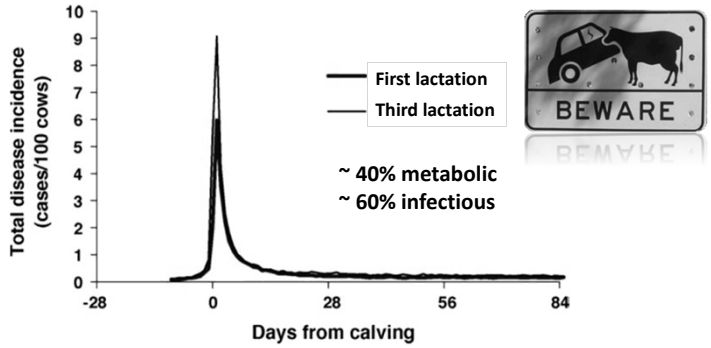
Overview

- Immunity and inflammation in the transition cow
- Long-lasting effects of early lactation problems
- Predicting transition train wrecks
- Disrupting pathology

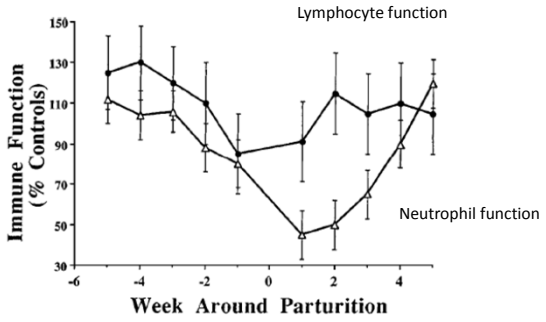


The transition period



Ingvartsen, 2006

Transition cows have decreased immune function



Goff and Horst,1997

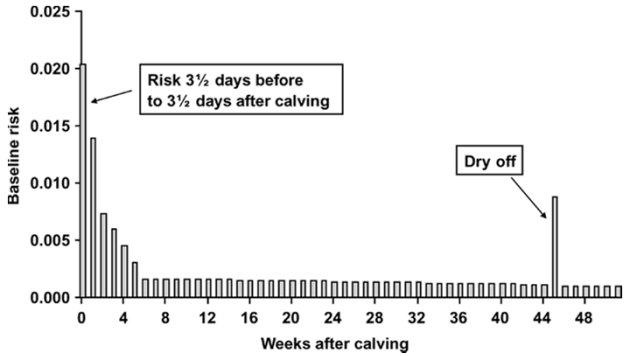
Transition immune cells

- Enhanced inflammatory response
- Impaired chemotaxis
- Decreased phagocytosis
- Reduced killing ability

All talk!

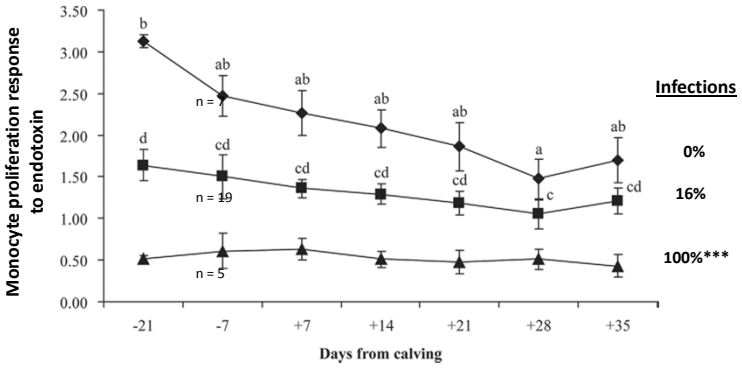
Sordillo et al., 1995; Contreras et al., 2012; Kehrli et al., 1989; Nonnecke et al., 2003

Immunosuppression coincides with greater risk of infection



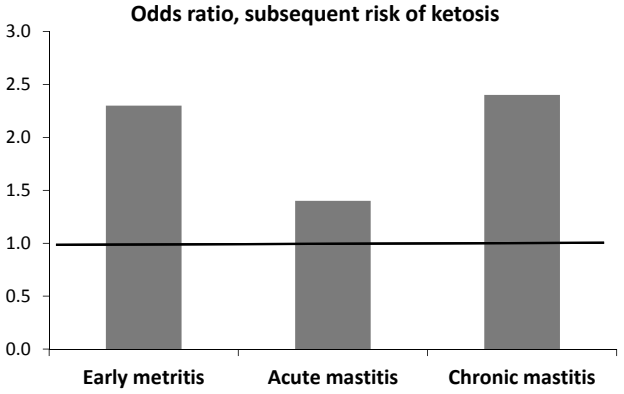
Østergaard et al, 2005

Immune function predicts infection risk



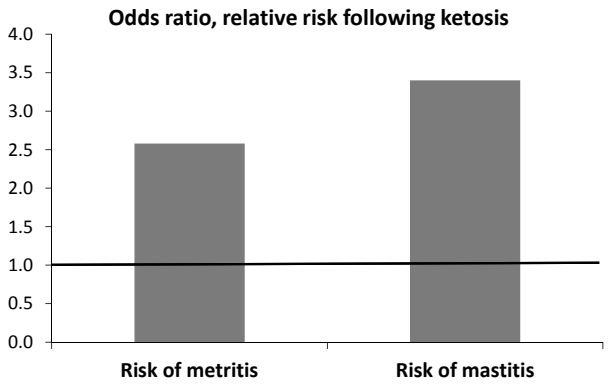
Catalani et al, 2013

Infections increase ketosis risk



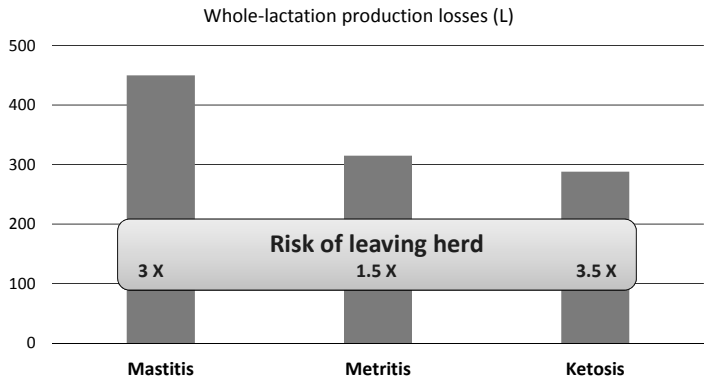
Gröhn et al., 1989

Ketosis increases infection risk



Duffield et al., 2009; Doohoo and Martin, 1984

Long-term consequences of transition problems



Seegers 2003; Deluyker 1991; Wittrock 2011; Ospina 2010; Seifi 2011

- ✓Suppressed **immune function** contributes to infectious disorders
- ✓Infections promote **metabolic disorders**
- ✓Metabolic problems increase **infection risk**

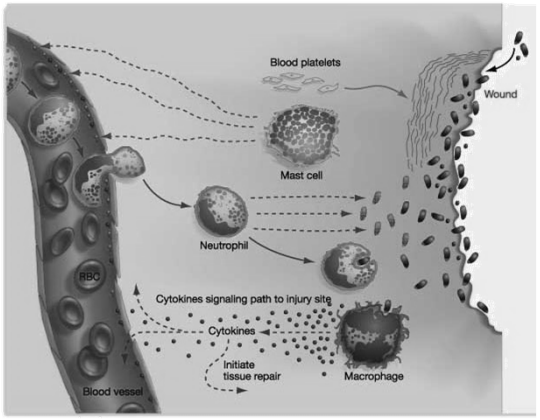
Does inflammation provide a mechanistic link?

Inflammation

Acute inflammation

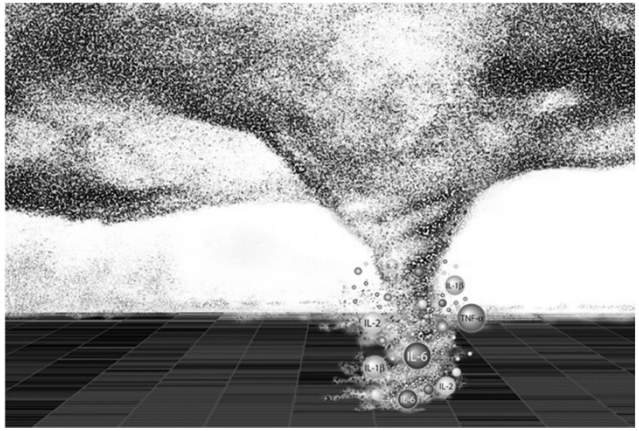
- Associated with immune activation or tissue damage
- Swelling
- Pain
- Fever

Innate immune response



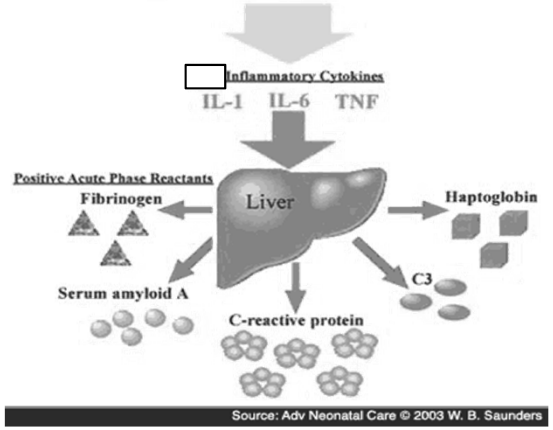
www.uic.edu/classes/bios/bios100/lecturesf04am/lect23.htm

The cytokine storm



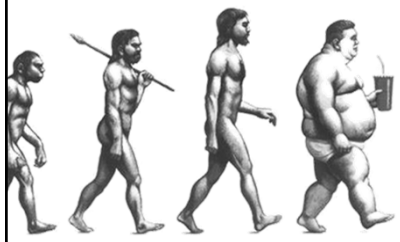
Tisoncik J R et al. Microbiol. Mol. Biol. Rev. 2012;76:16-32

INFLAMMATION



Source: Adv Neonatal Care © 2003 W. B. Saunders

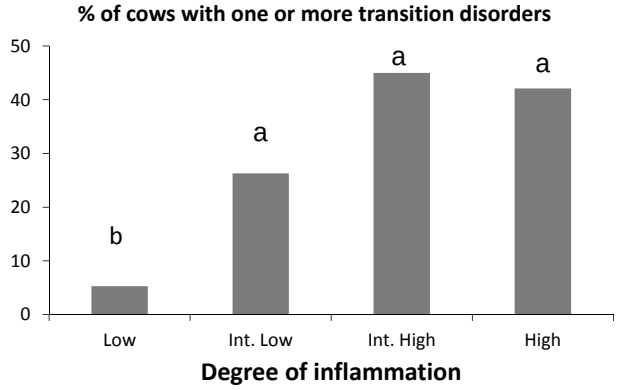
Inflammation



Chronic inflammation

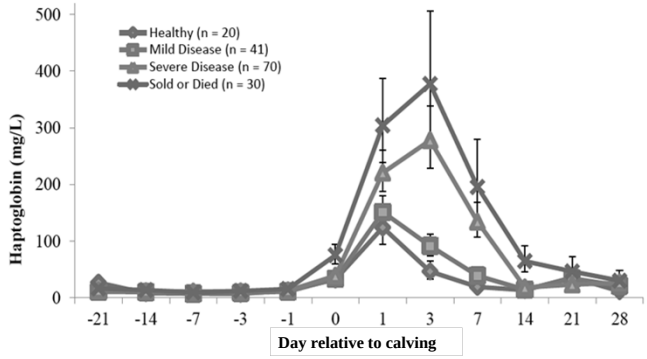
- No outward signs
- Slightly elevated inflammatory mediators
- Alterations in signaling

Inflammation is associated with transition disorders



Bertoni et al., 2008

Subacute, liver inflammation is common in postpartum cows



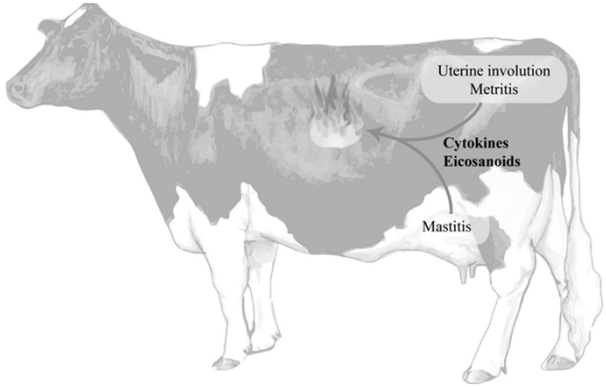
Sabedra, 2012 (thesis)

What causes transition inflammation?

Systemic inflammation

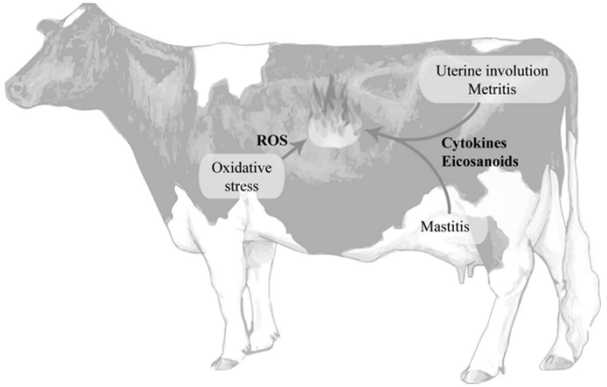
Bradford et al., 2015

Systemic inflammation



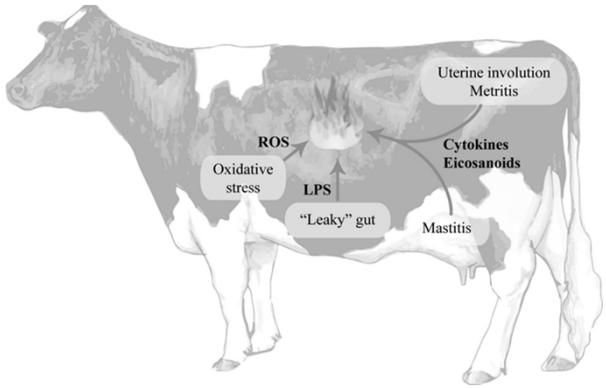
Bradford et al., 2015

Systemic inflammation



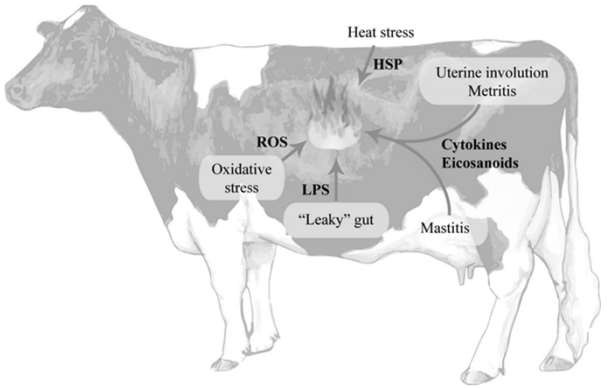
Bradford et al., 2015

Systemic inflammation



Bradford et al., 2015

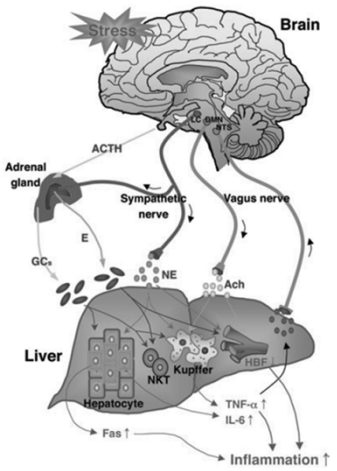
Systemic inflammation



Bradford et al., 2015

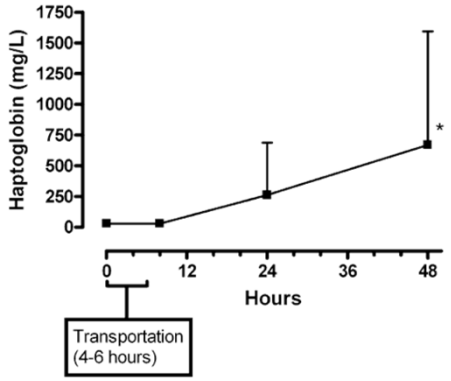
Stress hormones

- Physiological levels of glucocorticoids, epinephrine, and norepinephrine may promote liver inflammation



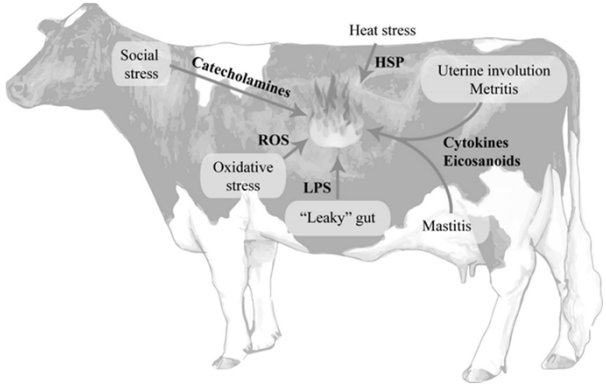
Chida et al., 2006

Handling stress induces an acute phase response in cattle



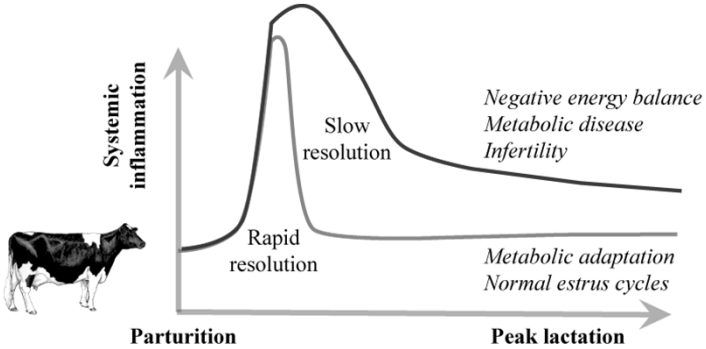
Lomborg et al., 2008

Systemic inflammation



Bradford et al., 2015

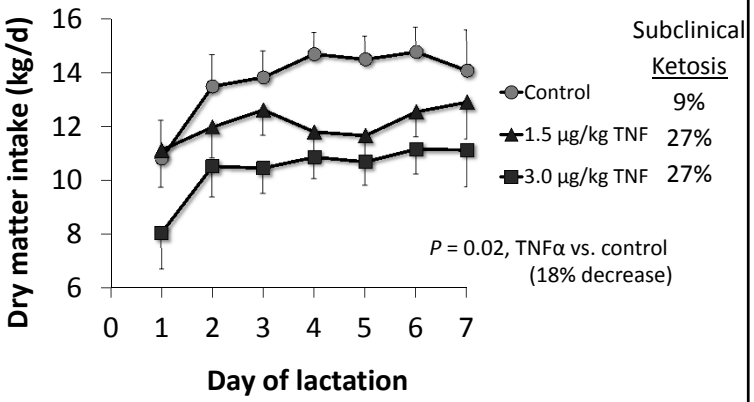
Hypothetical impacts of *unresolved* inflammation



Bradford et al., 2015

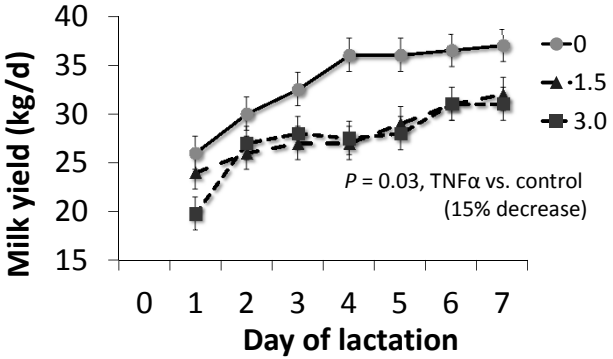
How does this impact cows?

Inflammation promotes ketosis



Yuan et al., 2013

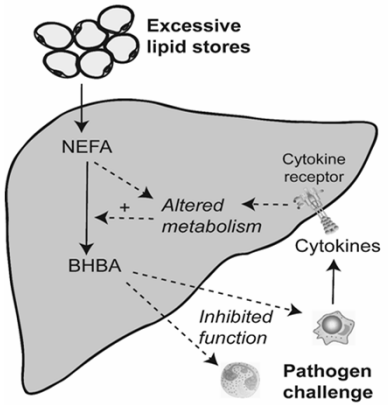
…and decreases milk yield



Yuan et al., 2013

A vicious cycle

Metabolic disorders
promote
Infections
promote
Metabolic disorders

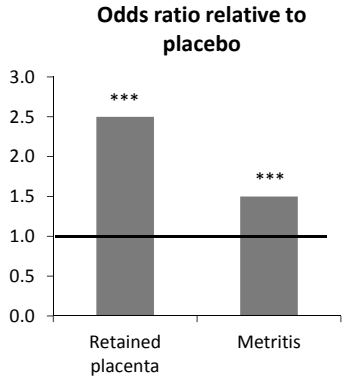


Should we block inflammation?

Immediate postpartum NSAID

- Flunixin meglumine given 2 h and 24 h after calving
- Over 1,300 cows enrolled

Blocking inflammation on the day of calving may interfere with inflammatory signals needed to expel the placenta



Duffield et al., 2009

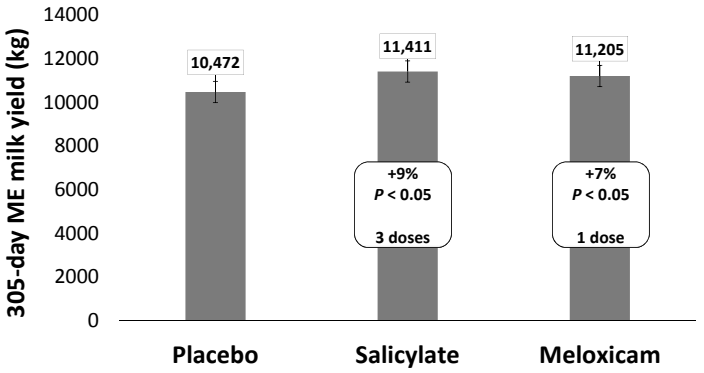
Delayed Treatment: On-farm NSAID study

1. Na salicylate
2. Meloxicam

- Administered orally starting 24 h postpartum
- 51 multiparous cows per treatment

Carpenter et al., 2016

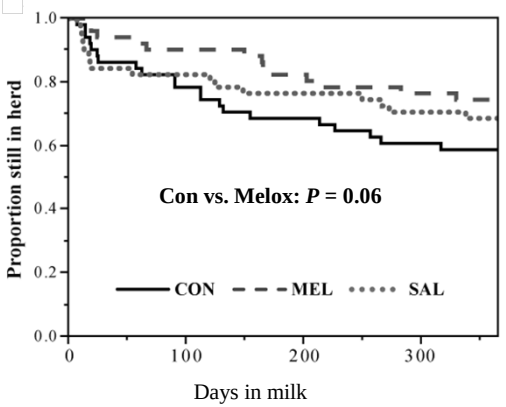
Anti-inflammatories in early lactation (not currently approved)



Carpenter et al., 2016

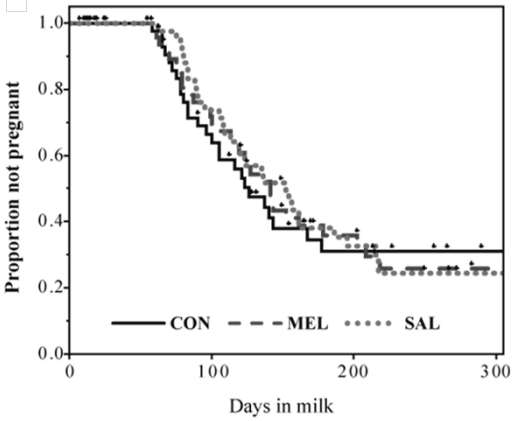
Too much milk?

Time to Leave Herd



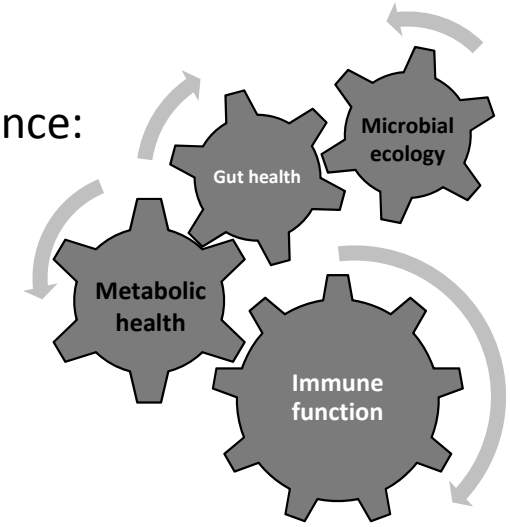
Carpenter et al., 2016

Time to Pregnancy

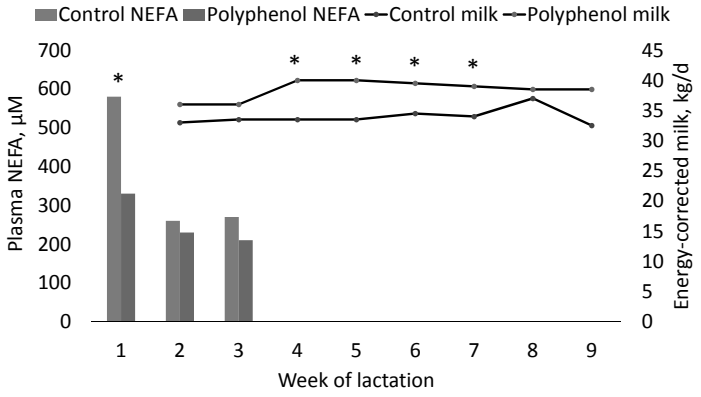


Carpenter et al., 2016

Nutrition can directly influence:

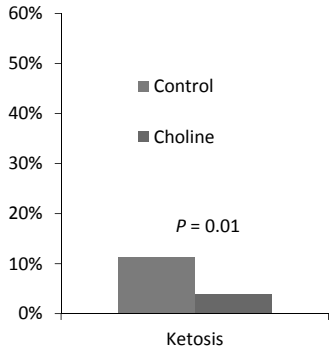


Polyphenol source improves the transition



Winkler et al., 2015

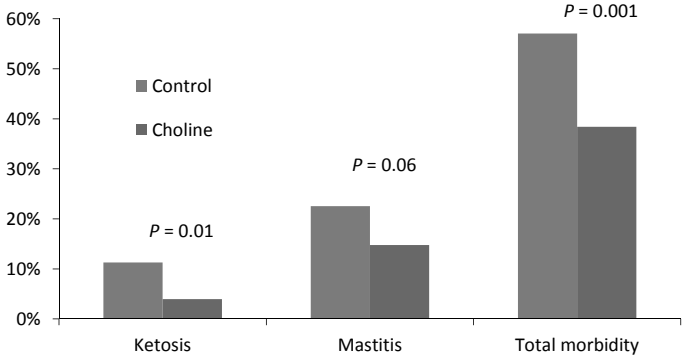
Unexpected benefits?



Cows were fed 15 g choline per day from 25 days before calving to 80 days in milk.

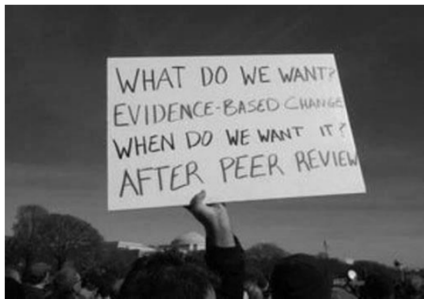
Lima et al., 2012

Unexpected benefits?



Lima et al., 2012

Best practices to support immunity?



Best practices to support immunity?

- Prevent heat stress during the dry period
- Calve with a BCS ≤ 3.5
- Supplement with antioxidants during the dry period
- Work to maintain postpartum total serum calcium concentrations near 9 mg/dL
- Work to keep postpartum blood BHBA and NEFA concentrations below 1 mM

The Big Picture

- There is much crosstalk between metabolic and immune systems
- Inflammatory signals, driven by a wide variety of stimuli, are a key link
  - Not always a negative
- The physiological milieu in the first week can have long-term impacts
- Strong immune function can help to prevent unresolved inflammation and long-term problems