Inflammation, Immune Function, and the Transition Cow

Barry Bradford
Kansas State University
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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

Transition cows have decreased immune function

Ingvartsen, 2006

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

Long-term consequences of transition problems

✓ 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
The cytokine storm

Chronic inflammation
- No outward signs
- Slightly elevated inflammatory mediators
- Alterations in signaling
Inflammation is associated with transition disorders

% of cows with one or more transition disorders

Bertoni et al., 2008

Subacute, liver inflammation is common in postpartum cows

Day relative to calving

Sabedra, 2012 (thesis)

What causes transition inflammation?

Systemic inflammation

Bradford et al., 2015
Stress hormones

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

Handling stress induces an acute phase response in cattle

Systemic inflammation

Hypothetical impacts of unresolved inflammation
How does this impact cows?

Inflammation promotes ketosis

A vicious cycle

Metabolic disorders promote infections

Metabolic disorders promote inhibited function

Pathogen challenge

Cytokines

Altered metabolism

BHBA

NEFA

Cytokine receptor

Excessive lipid stores

Yuan et al., 2013

Yuan et al., 2013

Yuan et al., 2013
**Should we block inflammation?**

Immediate postpartum NSAID

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

**Delayed Treatment: On-farm NSAID study**

1. Na salicylate
2. Meloxicam
   - Administered orally starting 24 h postpartum
   - 51 multiparous cows per treatment

**Anti-inflammatories in early lactation (not currently approved)**

Carpenter et al., 2016
Too much milk?

Time to Leave Herd

Con vs. Melox: $P = 0.06$

Time to Pregnancy

Nutrition can directly influence:

- Immune function
- Gut health
- Metabolic health
- Microbial ecology

Carpenter et al., 2016
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

Thank you!

Questions/comments:
Barry Bradford
bbradfor@ksu.edu
@AnimNutr