Enhancing Immunity Through Vitamin D

Outcomes of 2014-2015 Milk Check-Off Projects:
Minimizing Costs of Mastitis Through Enhancing Antimicrobial Protein Production in the Udder
-Awarded to Nelson and Santos

Use of 1,25 Vitamin D3 (Calcitriol) to Maintain Postpartum Blood Calcium (Ca) and Improve Immune Function in Dairy Cows
-Awarded to Santos and Nelson

Our goal: Minimize incidence of transition cow diseases.
Disease risk is minimized through proper nutrition and management.
But, nutrition and management are not always enough.

Transition Cow Health

Approach: Identify viable therapies that enhance immunity of transition cows.

Basic Research: Understand how the immune system works and what signals control immunity of the cow.

Applied Research: Test the effectiveness of immune modulating therapies that have potential for on-farm use.

Vitamin D, Calcium and Immunity

Vitamin D3
Calcium

Improved Immunity
Disease Resistance
Vitamin D, Calcium and Immunity

Vitamin D₃ → 25-Hydroxyvitamin D₃ → 1,25-Dihydroxyvitamin D₃ → Active → Improved Immunity → Disease Resistance

Calcium

Vitamin D helps activate antimicrobial defenses

Vitamin D contributes to activation of antimicrobial defenses in the mammary gland.

Hypothesis:

Objective:

Determine the effects of intramammary 1,25D treatment on induction of host defenses in the udder to understand mammary immunity.

Isolate Milk Somatic Cells → Measure Gene Expression

14 cows

1,25D₃ Placebo

Inos mRNA

Nitric oxide production

P < 0.001, n = 6

25(OH)D₃ dose (ng/ml)


Nature Reviews Immunology 3, 710-720 (September 2003)

Bovine β-defensins


Monocyte DEF3B mRNA

Monocyte DEF7B mRNA
Hypothesis:
Vitamin D contributes to activation of antimicrobial defenses in the mammary gland... During mastitis

Objective:
Determine the effects of intramammary 1,25D treatment on induction of host defenses in subclinically infected glands.

1,25D3 or Placebo
Treatment repeated after each milking for 5 milkings (every 12 h)

Responses to Intramammary 1,25D Treatment
Gene Expression in Milk Somatic Cells

- iNOS
  - P = 0.023
- bBD3
  - P = 0.179
- bBD4
  - P = 0.366
- bBD6
- bBD7
  - P = 0.029
- bBD10

15 cows
Isolate Milk Somatic Cells → Measure Gene Expression

Gainesville, FL, April 6, 2016

Nelson, 2016 Florida Dairy Production Conference
Responses to Intramammary 1,25D Treatment: During Subclinical Mastitis

Gene Expression in Milk Somatic Cells

Conclusions:
- Activated vitamin D stimulates antimicrobial responses of cattle.

Implications:
- Vitamin D requirement for immunity
- Therapeutic potential for vitamin D compounds in treatment of mastitis
Vitamin D, Calcium and Immunity

Calcium

Vitamin D<sub>3</sub>

25-Hydroxyvitamin D<sub>3</sub>

25(OH)D<sub>3</sub>

1,25-Dihydroxyvitamin D<sub>3</sub>

1,25(OH)<sub>2</sub>D<sub>3</sub>

Active

Improved Immunity

Disease Resistance

Circulating calcium is tightly regulated

Hypocalcemia

Hypocalcemia Suppresses Immunity

Immune cells require calcium to detect and eliminate pathogens

Onset of lactation causes transient decrease of calcium in circulation


Nelson, 2016 Florida Dairy Production Conference
Hypocalcemia

Risk of metritis increases with decreased calcium

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Solutions to Hypocalcemia

- Control of sustained circulating calcium is complex
- Not as simple as providing more calcium
- Tightly controlled endocrine mechanisms
- Requires increases in absorption, retention, and mobilization of calcium

- Calcium Mobilization
- Calcium Absorption
- Calcium Retention

Bone Small intestine Kidney

Role of Vitamin D

Impaired even with good management

25-vitamin D₃ → Low Ca → 1,25-vitamin D₃

Inactive → Active

- Calcium Mobilization
- Calcium Absorption
- Calcium Retention

Bone Small intestine Kidney

Use of 1,25 Vitamin D3 (Calcitriol) to Maintain Postpartum Blood Calcium (Ca) and Improve Immune Function in Dairy Cows

Achilles Vieira-Neto and Jose E.P. Santos
University of Florida, Gainesville, USA

Nelson, 2016 Florida Dairy Production Conference

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Gainesville, FL, April 6, 2016
Experimental Design

- Fifty cows fed negative DCAD prepartum
- Randomized to receive subcutaneous
  - Placebo
  - 300 μg 1,25-vitamin D
- Treatments given within 12 h of calving
- Measured responses of:
  - feed intake,
  - milk yield,
  - energy balance,
  - blood minerals,
  - neutrophil function

Effects of Post-Partum 1,25D on Minerals

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<th>Ionized Calcium</th>
<th>Total Calcium</th>
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<tr>
<th>Magnesium</th>
<th>Phosphorous</th>
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Effects of Post-Partum 1,25D on Neutrophils

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<tr>
<th>% Phagocytosis</th>
<th>% Oxidative Burst</th>
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Use of 1,25 Vitamin D3 (Calcitriol) to Maintain Blood Calcium (Ca) and Improve Immune Function

Conclusions:
- 300 ug of 1,25D given immediately post-partum prevents subclinical hypocalcemia
- The 1,25D treatment increased neutrophil phagocytosis and oxidative burst

Implications:
- Improved calcium and immunity status will lead to decreased transition cow diseases
- Potential adjunctive therapy to good transition cow management

Vitamin D Status of Dairy Cattle
Do dairy cattle get enough vitamin D?

Distribution of Serum 25(OH)D

YES
- Cows sampled from 10 herds fed 30,000 IU to 50,000 IU per day
- No benefit achieved beyond 50,000IU per day

Summary
- Intramammary 1,25D treatment boosts immune responses of the udder
- Post-partum subQ 1,25D treatment prevents subclinical hypocalcemia and boosts neutrophil function
- Better knowledge of what factors contribute to a strong immune system
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