Vitamin E and Selenium (and some other things) and Mastitis

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Good Nutrition

Maintain proper organ and cell functions

Strong Host Defense

Reduces immuno-suppressors

Good Nutrition

Healthier cows
Immuno-suppression

Around calving:
- PMN function
- Lymphocyte
- Macrophage

Kehrli, 2002
Parturition: High Risk for Mastitis

- Immuno-suppression
- Hypocalcemia
- Ketosis
- Overall low nutrient intake
- Antioxidant status (high oxidative stress)
“Nutritional Immuno-suppression”

1. Diets that promote high NEFA
2. Diets that promote ketosis
3. Diets that promote hypocalcemia

Preventing Metabolic Diseases via Good Nutrition improves immune function
High NEFA reduces Lymphocyte and Neutrophil function

**Lymphocytes from heifers**

**Fresh cow PMN Function**

Lacetera et al., 2004

Hammon et al., 2006
Bovine PMN Function Reduced with increased BHBA

Coliform Mastitis more Severe in Ketotic Cows

- Cows classified as normal or ketotic
- Infused with 1000 cfu *E. coli*
- Severity judged by cfu in gland over time

Kremer et al (1993) JDS 76:3428
Good Nutrition

Optimal system and cell functions

Strong Host Defense

Reduces immuno-suppressors

Healthier cows

Good Nutrition
Oxidative Stress:

\[ \text{[ROS]} > \text{Required} \]

* Antioxidant capacity

* Reactive \( O_2 \) Species (ROS*)

* Sometimes called free radicals
Reactive Oxygen Species (ROS)

Superoxide: \( O_2^\cdot \)

Singlet oxygen: \( ^1O_2 \)

Hydrogen peroxide: \( H_2O_2 \)

Hydroxyl radical: \( OH^\cdot \)

FA and peroxyl radicals: \( FA^\cdot \quad FA-OO^\cdot \)

Hypochlorous acid: \( HOCl \)

Hypothiocyanous acid: \( HOSCN \)
"Basal" Synthesis of Superoxide

\[ \text{O}_2 \rightarrow [\text{e}^-\text{TC}] \rightarrow \text{O}_2^- \rightarrow \text{H}_2\text{O}_2 \rightarrow \text{H}_2\text{O} \]

Mitochondria

Cytosol

(P450, etc.)

Endoplasmic reticulum
Metabolic Activity and ROS

650 kg nonlactating cow

Oxygen consumption: ~ 90 mol/d
Superoxide production: ~ 0.5 – 1.8 mol/d

650 kg lactating dairy cow (30 kg milk/d)

Oxygen consumption: ~230 mol/d
Superoxide production: ~1.1 – 4.6 mol/d
PMN: Activated ROS Synthesis

Migration

Phagocytosis

Kill

Oxidative burst

$O_2 \rightarrow O_2^\cdot \rightarrow$ Cytotoxic compounds

$O_2 \times 1,000,000$
Immune Cells and ROS

- Higher PUFA in membranes
- Bactericidal activity (high [ROS])

Membrane functions include:
- Antigen recognition
- Antibody secretion
- Phagocytosis

High PUFA + High ROS = 🤢
Oxidative Stress: \[ [\text{ROS}] > \text{Required} \]

Antioxidant capacity

Reactive \( O_2 \) Species (ROS)
Antioxidant Nutrients

- Selenium
- Vitamin E
- Copper
- Zinc
- B-carotene (?)
- Manganese
- Iron
- Vitamin C (?)

Often Deficient

Deficiency Unlikely
Nutritional Antioxidants

Cytosol

\[ \text{SOD} \quad \text{(Cu, Zn)} \quad \text{Catalase (Fe)} \quad \text{GSH-Px (Se)} \]

\[ \text{O}_2 \xrightarrow{\text{SOD}} \text{H}_2\text{O}_2 \xrightarrow{\text{GSH-Px}} \text{H}_2\text{O} \]

Membrane

\[ \text{FA} \xrightarrow{\text{BC}} \text{FA}^\cdot \xrightarrow{\text{Vit E}} \text{FA} \]

\[ \text{PH-GSHpx} \]

\[ \text{PL}^\cdot \xrightarrow{\text{Vit C}} \text{PL} \]

\[ \text{Vit C} \]

\[ \text{Vit C} \]

\[ \text{PL} \]

\[ \text{PL} \]

\[ \text{PH-GSHpx} \]
Selenium and vitamin E

Cytosol

Membrane

H$_2$O$_2$ \[\xrightarrow{\text{GSH-Px}}\] H$_2$O

FA \[\xrightarrow{\text{Vit E}}\] FA'

H$_2$O$_2$ \[\xrightarrow{\text{PH-GSHpx}}\] PL' \[\xrightarrow{\text{Vit E}}\] PL

FA \[\xrightarrow{\text{Vit E}}\] FA'
Selenite, vitamin E, and mastitis

Smith et al., 1984
Se/Vit E: Neutrophil kill (cattle)

O₂ Prod. (n=7)

- Positive: 29%
- No effect: 71%

Kill (n = 6)

- Positive: 17%
- No effect: 83%

10/13 positive
Vitamin E and immuno-suppression

>1000 IU/d in prefresh helps immunity and mammary gland health (4 studies)

Kehrli, 2002

Weiss et al., 1990
Plasma Vitamin E

Weiss et al., 1997
Vitamin E and Periparturient Cows

Weiss et al., 1997

Baldi et al., 2000
Antioxidants and Immuno-suppression?

Expression/activity of important antioxidant enzymes in mammary gland is low in late gestation

Aitken et al., 2009 (JDS)
Vitamin E and Mastitis: Clinical Data

5 Studies: Improved mammary gland health
2 Studies: No effect
1 Study: Negative

Various studies (all confined cattle)
None vs. ~1000/500
None vs high at transition
~500 vs extra at transition
High during dry period

Both all-rac and RRR tocopherol
Clinical Mastitis and Vit E Fed during dry period: Mastitis first 100 d

Bouwstra et al., 2010
Does Form of Vitamin E Matter? (synthetic vs. ‘natural’)

Tocopherol has 8 isomers (positions 2, 4, 8)
- Natural is all 2R, 4R, 8R (RRR)
- Synthetic has 8 isomers (12.5% RRR)
Relative Value (all-rac vs RRR)
Cows fed 2500 IU/d E

Weiss et al., 2009

USP: 1.49X: Suggest 2.0X
1. Amount to feed
   - 6 to 10 mg/day: all adult cattle

2. Factors affecting inclusion rates
   - Sulfur, Ca, Fe

3. Selenite vs Se-yeast
Selenium

Dairy cows should consume 6 to 10 mg of Se/day

- increase calf survival
- reduce risk of RFM
- reduce risk of mastitis
**E. coli** mastitis and Se

Erskine et al., 1989
Se and SCC

- Herds had low SCC
- Mostly environmental mastitis
- High plasma Se = lower BT SCC

Weiss et al., 1990
Nutrient Interactions

- Low Se: ↑ vitamin E
- Very high A: ↑ vitamin E
- High Fe: ↑ vitamin E and Se
- High sulfate: ↑ Se
- High/low Ca: ↑ Se
Se and Sulfur

-3% units/0.1% added S

Ivancic and Weiss, 2001
Se-yeast vs. selenite

Organic Se is different from all other organic trace minerals

All other organic TM are 'complexes'

\[ AA^- * AA^- * AA \]

\[ +Cu^+ \]

Organic Se is covalently bound in a molecule
Seleno-Amino Acids

Cysteine

Methionine

Se-cysteine

Se-methionine

Active center in selenoenzymes
# Se Compounds in Supplements

<table>
<thead>
<tr>
<th>Se-yeast</th>
<th>Selenite</th>
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</thead>
<tbody>
<tr>
<td>Se-met (50-98%*)</td>
<td>Selenite (100%)</td>
</tr>
<tr>
<td>Se-cys</td>
<td></td>
</tr>
<tr>
<td>Methyl Se compounds</td>
<td></td>
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<tr>
<td>Se-cys metabolites</td>
<td></td>
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<tr>
<td>Selenite (&lt;1%†)</td>
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</table>

* Wide range is probably analytical issue

† Reputable manufacturer (if Se-yeast cheap, may be contaminated with selenite)
Se Metabolism 101

Diet → Selenate → Selenite → Selenide

Se-met → General proteins

Selenide → Se-cys → Gen. proteins

Se-cys-tRNA_{UGA} → Se-specific proteins

Serine-tRNA_{UGA}
Selenate vs. Se-Yeast

Weiss and Hogan, 2006

Malbe et al., 1995
Which is better and how much better

Digestibility: Se-yeast 1.3 (?) X selenite
Blood / GSH-px: Se-yeast 1.2 X selenite
Fetal/calf: Se-yeast 1.4 X selenite
Milk: Se-yeast 1.9 X selenite
Immune function: Little difference (?)
Clinical response: Little difference (??)
Dry cow: Se-yeast should increase fetal/colostrum Se → calf health

Dietary antagonists (e.g., sulfate)

Se-yeast might be better (different absorption mechanisms)
Se Recommendations

Lactating cows, normal situation
- all or predominantly inorganic

Lactating cows, antagonists
- substantial amount from Se-yeast

Late gestation cows and heifers
- mix of inorganic and Se-yeast
Selenium: How Much?

Kommisrund et al., 2005

Whole blood = 0.16 - 0.18 (Se-yeast?)
## Determining Se adequacy

Units are mg/L

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<thead>
<tr>
<th></th>
<th>Plasma</th>
<th>Whole blood</th>
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<tbody>
<tr>
<td><strong>Adequate</strong></td>
<td>&gt;0.075</td>
<td>&gt;0.175</td>
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<tr>
<td><strong>Marginal</strong></td>
<td>0.05 to 0.075</td>
<td>0.13 to 0.175</td>
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<tr>
<td><strong>Deficient</strong></td>
<td>&lt;0.05</td>
<td>&lt;0.13</td>
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Based on mastitis and RFM
Recommendations for Vitamin E

1. Increase vitamin E for prefresh cows
   - 2000 to 4000 IU/d

2. NRC recommendations for far-off and lactating cows appear adequate

3. Pasture is great source of E, reduce or eliminate E supplementation