Using the Immune System to Maximize Cattle Profitability

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Director Cattle-Equine Immunology and Biologics
UN warns of looming worldwide food crisis

- Global grain reserves hit critically low levels
- Extreme weather means climate 'is no longer reliable'
- Rising food prices threaten disaster and unrest

The Guardian  October 13, 2012
America Has Lost More Than 23 Million Acres of Agricultural Land in Last 25 Years

New data from the federal government's latest NRI survey shows every state is losing prime farmland.

Published on: May 4, 2010
At times, you can make almost anything work!
Vaccination Program

* nutrition
* genetics
* environment
* management programs
Bovine Bacterial Pneumonia

Shipping Fever –
Major cause of death, clinical disease and economic losses in the beef cattle industry

Enzootic Pneumonia –
Second most severe disease of dairy calves
Cost of Respiratory Disease

For calves treated before 3 months of age

• 2.5 x more likely to die after 3 months (Waltner-Toews et al, 1986)

• 2.4 times more likely to die between 3 mo – 2½ yrs of age than heifers that had not been treated & had reduced growth during the first 6 months of life (up to 22 lb) (VanDerFels-Klerx, et al, NJAS, 2002)

• 2.4 x more likely to experience dystocia & Calve two months later (Warnick et al, 1994)
Calf Diarrhea

• Number one cause of economic loss in dairy calves
• Number two economic loss in beef calves

• What About Sickness, Treatments and Milk Yield?
  • 1st lactation milk yield was not significantly affected by reported cases of diarrhea
  • However, antibiotic treatment had a significant effect on TDM residual milk
  • Calves that were treated with antibiotics, produced 1,087 lbs less milk in the first lactation (P >0.01) than calves with no record of being treated

Soberon et al., 2012
STRESS
Factors Impacting the Immune Response

• Stress
  – Four different mechanisms
• Immunosuppresive diseases
  – BVDV, IBRV, Coccidia
• Development
• Aging
Stress & immune dysfunction summary

• Typically transient effects
• Delays inflammation by reducing efficiency of CD62L-mediated immune surveillance by neutrophils
• Decreased phagocytic cell function
• Increases trafficking of \( \gamma \delta \) T cells into epithelial sites
• Delays or impairs response to vaccines:
  – Decreases IFN-\( \gamma \) secretion by lymphocytes
  – Decreases antibody production by B-cells - e.g., impairs anamnestic response to vaccines
  – May decrease antigen presentation efficiency
Nutrition and stress, Do we really know what they are absorbing?

Figure 3. The dotted line extends from the tuber coxae to the elbow. The shaded box in the 10th intercostal space indicates the area for needle insertion.
Young calf thermoneutral zone 53.6°F-71.6°F
Is it hot outside?

Shut Up

DAIRY WELLNESS MAKES A DIFFERENCE.
Avoid Vaccinating >85°F

Don’t vaccinate at >85°F (29.4C) as this will increase the possibility of adverse reactions.

Be aware of night time lows 75°F (23.8C)
Calving Immunosuppression

- If possible, perform open cow vaccinations at days 14-30
- Vaccination immediately after calving is catching the cow at an immunosuppressive low point
- Likewise, don’t vaccinate the calf with a modified-live during the 1\textsuperscript{st} week of life (exception TSV-2\textsuperscript{®} and CALF-GUARD\textsuperscript{®})
Diminished IFN-γ and Blastogenic responses in the first few days after birth, in neonatal calves
Colostrum

• IgG selectively transported to the mammary gland and concentrated by 5X\(^1\)
  – Concentration of immunoglobins in mammary gland begins 5 weeks prior to calving and peaks 2 weeks precalving\(^2\)
  – One study 2 weeks with a peak 48 hours precalving\(^3\) - artificial induction of lactation

• Cow systemic IgG antibodies may drop by up to 50% during this period

• Calf absorption of colostral antibodies will end up approximating the precolostral titer of the cow

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2 Morrow. *Current Therapy in Theriogenology.*
Vaccination for Calf Protection

First Time

- Serum IgG
- Colostrum IgG

Primary Response
- Min 2Wk
- 1st Vac.
- 2nd Vac.
- 2nd Vac.
- 4 Weeks
- Min 3Wk

Secondary Response
- Min 3Wk
- 4 Weeks
- 6 Weeks

IgG Transfer To Colostrum
- Min 3Wk
- 6 Weeks
- 8 Weeks
- 10 Calving
Australia ScourGuard 4K study

• Series of studies supporting registration of Scourguard 4K in New Zealand
• Presented at Australian Veterinary Congress in 2014

First study compared intervaccination interval and antibody response

Second study compared antibody responses of two doses of Scourguard versus a one dose booster and placebo administered approximately one year later
Two dose results and varying intervaccination interval

• Heifers vaccinated either 5 weeks between the initial two doses or vaccinated 9 weeks between the initial two doses
• One group was administered placebo vaccines on all three time
Table 1: Geometric Mean Serum Bovine Coronavirus Antibody Titers

<table>
<thead>
<tr>
<th>Day of Study</th>
<th>Negative control (n=15)</th>
<th>ScourGuard 4K™ (vacc 12 weeks and 9 weeks precalving) (n=30)</th>
<th>ScourGuard 4K™ (vacc 18 weeks precalving and 9 weeks precalving) (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 weeks precalving</td>
<td>1383&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1988&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>1725&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>12 weeks precalving</td>
<td>630&lt;sup&gt;a&lt;/sup&gt;</td>
<td>609&lt;sup&gt;a&lt;/sup&gt;</td>
<td>776&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>9 weeks precalving</td>
<td>437&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1290&lt;sup&gt;b&lt;/sup&gt;</td>
<td>506&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>8 weeks precalving</td>
<td>483&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1867&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1552&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>6 weeks precalving</td>
<td>482&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1320&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1176&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>3 weeks precalving</td>
<td>448&lt;sup&gt;a&lt;/sup&gt;</td>
<td>895&lt;sup&gt;b&lt;/sup&gt;</td>
<td>841&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Day of calving</td>
<td>309&lt;sup&gt;a&lt;/sup&gt;</td>
<td>446&lt;sup&gt;b&lt;/sup&gt;</td>
<td>456&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a, b, c</sup> Row means not sharing a common superscript are significantly different at the .05 level
## Table 2: Geometric Mean Serum Bovine Rotavirus G6 Antibody Titers

<table>
<thead>
<tr>
<th>Day of Study</th>
<th>Negative control (n=15)</th>
<th>ScourGuard 4K™ (vacc 12 weeks and 9 weeks precalving) (n=30)</th>
<th>ScourGuard 4K™ (vacc 18 weeks precalving and 9 weeks precalving) (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 weeks precalving</td>
<td>536^a</td>
<td>438^a</td>
<td>354^a</td>
</tr>
<tr>
<td>12 weeks precalving</td>
<td>416^a</td>
<td>397^a</td>
<td>978^b</td>
</tr>
<tr>
<td>9 weeks precalving</td>
<td>698^a</td>
<td>2025^b</td>
<td>1415^b</td>
</tr>
<tr>
<td>8 weeks precalving</td>
<td>666^a</td>
<td>6353^b</td>
<td>7383^b</td>
</tr>
<tr>
<td>6 weeks precalving</td>
<td>376^a</td>
<td>3484^b</td>
<td>3956^b</td>
</tr>
<tr>
<td>3 weeks precalving</td>
<td>366^a</td>
<td>1742^b</td>
<td>2380^b</td>
</tr>
<tr>
<td>Day of calving</td>
<td>306^a</td>
<td>841^b</td>
<td>1072^b</td>
</tr>
</tbody>
</table>
### Table 3: Geometric Mean Serum Bovine Rotavirus G10 Antibody Titers

<table>
<thead>
<tr>
<th>Day of Study</th>
<th>Negative control (n=15)</th>
<th>ScourGuard 4K™ (vacc 12 weeks and 9 weeks precalving) (n=30)</th>
<th>ScourGuard 4K™ (vacc 18 weeks precalving and 9 weeks precalving) (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 weeks precalving</td>
<td>489&lt;sup&gt;a&lt;/sup&gt;</td>
<td>417&lt;sup&gt;a&lt;/sup&gt;</td>
<td>418&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>12 weeks precalving</td>
<td>467&lt;sup&gt;a&lt;/sup&gt;</td>
<td>431&lt;sup&gt;a&lt;/sup&gt;</td>
<td>785&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>9 weeks precalving</td>
<td>1045&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>1367&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1190&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>8 weeks precalving</td>
<td>759&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3692&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3911&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>6 weeks precalving</td>
<td>704&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2551&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2671&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>3 weeks precalving</td>
<td>656&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1588&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1626&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Day of calving</td>
<td>658&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1024&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1110&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
Table 4: Geometric Mean Serum *E. coli* K99 Antibody Titers

<table>
<thead>
<tr>
<th>Day of Study</th>
<th>Negative control (n=15*)</th>
<th>ScourGuard 4K™ (vacc 12 weeks and 9 weeks precalving) (n=30)</th>
<th>ScourGuard 4K™ (vacc 18 weeks precalving and 9 weeks precalving) (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 weeks precalving</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>12 weeks precalving</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>478&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>9 weeks precalving</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>436&lt;sup&gt;c&lt;/sup&gt;</td>
<td>177&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>8 weeks precalving</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>13004&lt;sup&gt;b&lt;/sup&gt;</td>
<td>11585&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>6 weeks precalving</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6069&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6208&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>3 weeks precalving</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2641&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2641&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Day of calving</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1098&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1261&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
Conclusions of study one

• No difference in antibody levels in heifers post vaccination if vaccinated 3 weeks or 9 weeks apart with their initial series 9 weeks takes you back to approximately 5 months of pregnancy)
• Antibody levels peaked ten day after booster administration
• Antibody levels began to decline 21 days post vaccination with the booster and continue to decline
Study two yearly booster

Heifers from first study were given either a single dose of Scourguard 4K or a placebo following a full lactation, approximately 12 months after the initial series.

Antibody levels were compared to two dose responses from the initial series.
Table 5: ScourGuard 4(K)™ Booster - Bovine Coronavirus Geometric Mean Serum Antibody Titers

<table>
<thead>
<tr>
<th>day of study</th>
<th>Negative control - adjuvanted placebo (n=12)</th>
<th>ScourGuard 4(K)™ Booster Vaccination at 12 months (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 weeks prior to calving</td>
<td>575&lt;sup&gt;a&lt;/sup&gt;</td>
<td>642&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>6 weeks prior to calving</td>
<td>664&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1218&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>4 weeks prior to calving</td>
<td>790&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1123&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
Table 6: ScourGuard 4(K)™ Booster - Bovine Rotavirus G6 Geometric Mean Serum Antibody Titers

<table>
<thead>
<tr>
<th>day of study</th>
<th>Negative control - adjuvanted placebo (n=12)</th>
<th>ScourGuard 4(K)™ Booster Vaccination at 12 months (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 weeks prior to calving</td>
<td>494 $^a$</td>
<td>1388 $^b$</td>
</tr>
<tr>
<td>6 weeks prior to calving</td>
<td>856 $^a$</td>
<td>6261 $^b$</td>
</tr>
<tr>
<td>4 weeks prior to calving</td>
<td>1048 $^a$</td>
<td>4687 $^b$</td>
</tr>
</tbody>
</table>
Table 7: ScourGuard 4(K)™ Booster - Bovine Rotavirus G10 Geometric Mean Serum Antibody Titers

<table>
<thead>
<tr>
<th>day of study</th>
<th>Negative control - adjuvanted placebo (n=12)</th>
<th>ScourGuard 4(K)™ Booster Vaccination at 12 months (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 weeks prior to calving</td>
<td>1085 (^a)</td>
<td>3222 (^b)</td>
</tr>
<tr>
<td>6 weeks prior to calving</td>
<td>1253 (^a)</td>
<td>6275 (^b)</td>
</tr>
<tr>
<td>4 weeks prior to calving</td>
<td>1448 (^a)</td>
<td>5966 (^b)</td>
</tr>
</tbody>
</table>
### Table 8: ScourGuard 4(K)™Booster - *E. coli* K99 Geometric Mean Serum Antibody Titers

<table>
<thead>
<tr>
<th>day of study</th>
<th>Negative control - adjuvanted placebo (n=12)</th>
<th>ScourGuard 4(K)™ Booster Vaccination at 12 months (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 weeks prior to calving</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>167&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>6 weeks prior to calving</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6435&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>4 weeks prior to calving</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3870&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
Study 2 conclusions

• By 12 months following calving baseline antibody levels were the same in unvaccinated controls as previously vaccinated heifers
• A single yearly gave titers of the same level as two doses of vaccine
• Antibody levels peaked again at 10-14 days after vaccination and began to decline by 28 days post vaccination

•
The Bovine Placenta – more layers

Placentas can be classified based on which maternal layers are retained in the placenta. The bovine placenta has more layers than most other species.

<table>
<thead>
<tr>
<th>Type of Placenta</th>
<th>Maternal Layers Retained</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Endometrial Epithelium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Connective Tissue</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Uterine Endothelium</td>
<td></td>
</tr>
<tr>
<td>Epitheliochorial</td>
<td>+</td>
<td>Cows, horses, pigs, ruminants</td>
</tr>
<tr>
<td>Endotheliochorial</td>
<td>-</td>
<td>Dog, cats</td>
</tr>
<tr>
<td>Hemochorial</td>
<td>-</td>
<td>Humans, rodents</td>
</tr>
</tbody>
</table>
Colostrum

• Important for survival
• Concentrated source of proteins, vitamins (especially vitamin A), minerals, sugar
• Contains antibodies - only protection newborn calves have
• Laxative
• Must give enough early
• Stimulation of calf’s own immunity
Colostrual Constituents Continued

- IGF-I – local gut effects
- IGF-II – local gut effects
- Lactoferrin – local immunity effect in gut
- Leptin – could affect the hypothalamic pituitary axis
- Prolactin – little data but good candidate for calves
- Insulin – local gut effects
- Leptin – could affect the hypothalamic pituitary axis
- Relaxin – humans, dogs, pigs – reproductive development
- Essential and non-essential amino acids
- Fatty acids – wide profile of fatty acids
Colostrum has long term impacts on growth, health and production
Calves fed
2 or 4 qts of colostrum at birth

<table>
<thead>
<tr>
<th>Treatment (qts)</th>
<th>No. of calves</th>
<th>Health Disorders</th>
<th>Cull Rate (%)</th>
<th>Veterinary cost per calf ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>37</td>
<td>8(^1)</td>
<td>24.3</td>
<td>24.51</td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>5(^2)</td>
<td>12.9</td>
<td>14.77</td>
</tr>
</tbody>
</table>

\(^1\)Pneumonia (n = 3), ulcers (2), poor health (3)
\(^2\)Corona virus (4), navel infection (1)

Faber, et al., 2005. Prof. Animal Sci. 21:420
Age at conception and daily gain of Brown Swiss heifers fed 2 or 4 qts of colostrum at birth

<table>
<thead>
<tr>
<th>Treatment (No. calves)</th>
<th>Age (mo) at conception</th>
<th>ADG,^1 lbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 q (37)</td>
<td>13.97^a</td>
<td>1.8^a</td>
</tr>
<tr>
<td>4 q (31)</td>
<td>13.54^a</td>
<td>2.3^b</td>
</tr>
</tbody>
</table>

^1Weights were estimated from heart girth measurements; ADG was computed by dividing weight (minus initial body wt) by day of age. ^a,bValues with different superscripts within a column differ (P < 0.001).

Faber, et al., 2005. Prof. Animal Sci. 21:420
Effect of Colostrum on 305-d ME Milk

Heifers receiving 4 L produced 2 lb more per day over two lactations

Faber, et al., 2005. Prof. Animal Sci. 21:420
Calf Colostrum Absorption

Percent

Hours
Declining IgG in Colostrum Following Calving
13 cows/52 quarters

Reason for effect?

- not due to dilution (same volume from all quarters at each time point)

- possibly due to reabsorption into maternal circulation

Moore, et al., 2005 JAVMA 226:1375
Colostral Leukocytes

- $10^6$ leukocytes per milliliter of colostrum comprised of:
  - Macrophages
  - Neutrophils
  - Lymphocytes 10,000/ml
    - T-cells 9,700/ml
    - B-cells 300/ml

Colostral Leukocytes

• Regulate and enhance defense mechanisms
  – Lymphocyte responses
  – Passive immunity
  – Phagocytosis
  – Bactericidal
  – Transfer cell-mediated immunity

Assessing Failure of Passive Transfer — Days 3 – 10

<table>
<thead>
<tr>
<th>Test</th>
<th>Failure of Transfer</th>
<th>Partial Failure</th>
<th>Adequate Transfer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein</td>
<td>5.0 g/dl</td>
<td>5-6 g/dl</td>
<td>&gt;6 g/dl</td>
</tr>
<tr>
<td>Sodium sulfite</td>
<td>0-7</td>
<td>8-16</td>
<td>&gt;16</td>
</tr>
<tr>
<td>Radial immunodiffusion</td>
<td>&lt;800 mg/dl</td>
<td>800-1600 mg/dl</td>
<td>&gt;1600 mg/dl</td>
</tr>
<tr>
<td>Zinc turbidity</td>
<td>0-1</td>
<td>2-3</td>
<td>3-4</td>
</tr>
</tbody>
</table>

Dairy calves >5.5 generally considered adequate.
Colostral preparation

- Handling
  - Cleanliness
  - Proper cooling
  - No RBCs
  - Pasteurization
- Feeding
  - Proper temperatures and amounts
- Vaccinations to improve colostral quality
  - Timing is critical
  - Not all vaccines increase colostral antibodies and some may actually decrease overall colostral antibodies*

Brenner et al. Impact of vaccination of pregnant cows on colostral IgG levels and on term of pregnancy, field observations, Israel JVM, 52:2-3, 1997
Pro-active Calf Program Goals

• 1 Double birth weight by 56 days (minimum goal)
• 2 Calf mortality less than 5%
• 3 Calf morbidity (treatments) less than 10%

• Why Do This?
  • Capture feed efficiency of early life
  • Achieve breeding weight at an earlier age
  • Potentially reduce AFC/increase BW @ calving
  • Increase potential for Internal Herd Growth
  • Potentially increase milk yield and herd life
## Correlation of ADG Pre-weaning with Milk Production

**Lactation n** Predicted Difference in Milk per lb of Pre-weaning ADG

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Predicted Difference in Milk per lb</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>1,244</td>
<td>849.6 (216.3)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>2nd</td>
<td>826</td>
<td>888.1 (310.1)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>1st to 3rd</td>
<td>450</td>
<td>2,279.5 (918.9)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Soberon et al., 2012
Nature vs. Nurture

In this study, 22% of the variation in first lactation milk yield was explained by pre-weaning ADG.

No genetic trait accounts for as much variation yield 22.

Sire selection for milk results in 150 to 250 lb milk per lactation.

This suggests that pre-weaning nutrient intake is responsible for up to 7 times more milk per lactation than sire selection for milk yield.

Soberon et al., 2012
A Mature Immune System

Consider the immune system to be mature by 10-12 months of age.

Some maternal antibody may persist at this time, so consider a 2nd MLV BVD vaccination prebreeding.
Clinical disease is easier to protect against!

![Diagram showing protection levels over time following vaccination with IBR Abortion, BVD Type 1 and 2, Bvi-Shield FP, Fetal Protection Threshold, Respiratory Protection, Brands X, and Brands Y.](image)
Why and when are intranasals used

• Traditionally
  – Heavily stressed
  – young calves
  – In the face of disease outbreaks
  – Safety is a key component here
  – Used for immune modulation not for vaccination
    • Interferon release
Interferon Levels Post Challenge

- TSV vaccinated calves responded quickly to a virulent IBR challenge.
- Interferon levels appeared more quickly and at higher levels than calves vaccinates with an IM IBR vaccine.

# TSV2 or Conventional Intranasal Vaccine?

<table>
<thead>
<tr>
<th>Number of Calves</th>
<th>treatment</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>2500</td>
<td>TSV2</td>
<td>4.2%</td>
</tr>
<tr>
<td>2500</td>
<td>Traditional IN</td>
<td>5.5%</td>
</tr>
</tbody>
</table>

**Apparent Risk Reduction = 1.32%**  
**Relative Risk Reduction = 23.9 %**
What is Unique About the Intranasal Immune Response of INFORCE 3?

Bovine Respiratory Syncytial Virus

- The Immune Response
  - Replication occurs locally (aberrant replication occurs when administered systemically)
  - IgA trafficking to nasal passages
  - Cell mediated trafficking to nasal passages

- Fast stimulation of immune system

- CAN NOT be achieved any other way
When does BVDV vaccination begin

• Don’t Wait!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!
  – Particularly in south east cattle unless you want to have a bad day
When does BVDV vaccination begin

• BoviShield Duration of BVDV cross neutralization antibodies last 18 months post vaccination\(^1\)

Serology Results

Sentinel geometric mean serum virus neutralization antibody titers.

<table>
<thead>
<tr>
<th>Day</th>
<th>IBR</th>
<th>BRSV</th>
<th>BVD1</th>
<th>BVD2</th>
<th>PI3</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>16.5</td>
<td>34.0</td>
<td>506.6</td>
<td>196.8</td>
<td>114.4</td>
</tr>
<tr>
<td>28</td>
<td>26.4</td>
<td>77.9</td>
<td>990.5</td>
<td>323.9</td>
<td>151.7</td>
</tr>
<tr>
<td>49</td>
<td>9.9</td>
<td>31.8</td>
<td>214.0</td>
<td>80.5</td>
<td>47.8</td>
</tr>
<tr>
<td>63</td>
<td>8.0</td>
<td>16.3</td>
<td>156.1</td>
<td>57.1</td>
<td>33.0</td>
</tr>
<tr>
<td>84</td>
<td>5.5</td>
<td>19.3</td>
<td>171.4</td>
<td>47.6</td>
<td>15.2</td>
</tr>
<tr>
<td>105</td>
<td>4.5</td>
<td>19.1</td>
<td>142.0</td>
<td>37.2</td>
<td>21.4</td>
</tr>
</tbody>
</table>

Summarized but not analyzed.
What about intranasal vaccination in cows?
.7 lb increase in milk production for 305 day lactation
In poorer weather 3.5 lbs per day for 305 day lactation
Ongoing study in PA dairy

Inforce precalving (close ups)
Decreased mastitis
Decreased metritis
Decreased cull rates

Preliminary data
The Modified Live Advantage

• 1. Quicker onset of immunity than killed vaccines
• 2. Less adverse reactions
• 3. Stimulates a complete immune response
• 4. Mimics natural challenge so it gives a balanced immune response
• 5. Doesn’t require a booster dose
• 6. Longer duration of immunity
• 7. More stable in storage
But all modified lives are not the same!

• Differences in:
  – Protection
  – Safety
  – Duration
  – Ability to work in the young calf
Annual vaccination means one year of immunity!?
Annual revaccination means:

• We don’t know how long it lasts
• USDA does not require duration of immunity studies
• Studies successful at 14-35 days after vaccination are automatically given annual revaccination labels
## BHV-1 Duration for Reproduction Protection

<table>
<thead>
<tr>
<th>Product</th>
<th>Challenged</th>
<th>% IBR Abortions post vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Express</td>
<td>6 months</td>
<td>24%</td>
</tr>
<tr>
<td>• Vista</td>
<td>8 months</td>
<td>33%</td>
</tr>
<tr>
<td>• Virashield</td>
<td>7 months</td>
<td>14.3%</td>
</tr>
<tr>
<td>• BoviShield</td>
<td>12 months</td>
<td>5.3%</td>
</tr>
</tbody>
</table>

Published Duration Studies

Bovi-Shield GOLD®

• Duration of Immunity: Reproductive
  – Label; 12 months: Infectious Bovine Rhinotracheitis (IBR) Virus, Bovine Viral Diarrhea Virus (BVD) Types 1 & 2, and Lepto-hardjo bovis (LHB)
  – Reproductive Research
    • 16 month protection demonstrated against BVD Types 1 & 2¹
    • 12–17 month pregnant cow safety study (IBR abortions, BVD Infections and congenital defects)²
    • IBR 12 month DOI work compliments previous Bovi-Shield GOLD® data; vaccine is safe in pregnant animals that had been previously vaccinated in accordance with label directions³
    • Spirovac® data demonstrated no drop in protection 12 months after vaccination⁴
    • Duration of BVDV cross neutralization antibodies last 24 months post vaccination⁵
    • No adverse impact on reproduction or ovaries if previously vaccinated⁶

• Duration of Immunity: Respiratory
  – 279 days (over 9 months) for IBR, and BVD Types 1 & 2*


* When administered Subcutaneously
• Antibody levels do not equal reproductive protection against BVD, IBR or *L. borgpetersenii*
• Spirovac® has demonstrated prevention of uterine colonization, protection of the reproductive tract and subsequent improvements in reproductive parameters⁷
  – All others are licensed on impacts on the kidney
  – Spirovac has demonstrated lack of maternal interference⁸
• Bovi-Shield GOLD® studies have shown lack of maternal antibody interference against BRSV and IBR⁹,¹⁰
• Ongoing BVDV surveillance program
• What does this mean to vaccination programs?

⁹. Study Report No. 3131R-60-11-857, Pfizer Inc.
¹⁰. Study Report No. 3131R-60-09-667, Pfizer Inc.
How do we use this duration information?

Evaluation of Dry Cow Vaccination with a Killed Viral Vaccine on Post-colostral Antibody Titers in Calves

Jason B Osterstock, DVM; Robert J Callan, DVM, MS, PhD, DACVIM; David C. Van Metre, DVM, DACVIM
Colorado State University, Veterinary Teaching Hospital, Fort Collins, CO 80523

The results of the calf samples suggest that vaccination with a killed viral vaccine at the time of pregnancy confirmation in a herd that currently uses a modified-live vaccine after freshening offers no beneficial effects on post-colostral immune status in calves as measured by agent specific titers. Furthermore, the post-vaccination titers of the cows taken approximately 60 days after vaccination do not demonstrate a significant humoral immune response by the cows to the vaccine. This implies that the use of these killed vaccines does not stimulate a humoral immune response above that produced by annual vaccination with this modified-live viral vaccine.
Passive transfer of antibodies in pregnant cattle following vaccination with Bovi-Shield® FP® 5 L5. #12 Jacob Stegner1, MS; Glenn Alaniz1, BS; Todd Meinert1, MS, PhD; Guillermo, Gallo1, DVM, DVSc, PhD, MBA; Victor Cortese2, DVM, PhD; Pfizer Animal Health [(1)Veterinary Medicine Research and Development; (2)Veterinary Operations]

ABSTRACT
Two studies were conducted to evaluate the viral serologic response and passive transfer of antibodies in pregnant beef and dairy cows following vaccination with a commercial modified live vaccine (MLV) containing bovine herpesvirus 1 (BHV-1), bovine viral diarrhea virus (BVDV) types 1 and 2, parainfluenza virus type 3 (PI3) and bovine respiratory syncytial virus (BRSV) along with five serovars of leptospirosis (Bovi-Shield® GOLD® FP® 5 L5). All cows were previously vaccinated pre-breeding [dairy cows, Bovi-Shield GOLD® FP® 5 L5; beef cows, CalfMaster® GOLD® FP® 5 L5 killed virus (BVDV types 1 and 2), MLV (BHV-1, PI3, BRSV) and five serovars of leptospirosis]. Pregnant cows were randomized to either a non-vaccinated control group (dairy, N = 36; beef, N = 16; T1) or a vaccine group (dairy, N = 34; beef, N = 19; T2). Dairy cows were vaccinated at dryoff and the beef cows were vaccinated at 228-271 days of gestation (T2 only). Blood was collected from the cows at vaccination, calving and 10 days post-calving. Cows were monitored for signs of parturition and colostrum was collected pre-nursing. A calf blood sample was obtained pre- and three days post-colostrom intake. Serum and colostral virus neutralization (serum/SVN, colostral/CVN) antibody titers for BHV-1, BVDV types 1 and 2, PI3 and BRSV were evaluated for each time point.

RESULTS
None of the control animals were naturally exposed to the five viruses during the study as indicated by a lack of increase in SVN antibody titers. All calves retained in the analysis were seronegative (BHV-1, BVDV, PI3, SVN ≤ 1:2; BRSV SVN ≤ 1:8) pre-nursing. No adverse events were related to the vaccination.

Dairy: At calving vaccines exhibited significantly higher (P ≤ 0.05) geometric least squares mean (GLSM) SVN antibody titers for BHV-1 (T1 = 12.1 and T2 = 23.4), BRSV (T1 = 35.7 and T2 = 46.3) and PI3 (T1 = 116.9 and T2 = 183.2) when compared to controls. At 10 days post-calving, GLSM SVN antibody titers for vaccinated cows were significantly higher (P ≤ 0.05) for BHV-1 (T1 = 16.1 and T2 = 24.2) and PI3 (T1 = 103.1 and T2 = 169.9). The GLSM CVN antibody titers were significantly higher (P ≤ 0.05) for vaccinated dams versus controls for BHV-1 (T1 = 113.1 and T2 = 220.3), PI3 (T1 = 1159.7 and T2 = 2423.9) and BVDV2 (T1 = 1219.0 and T2 = 1830.7). At three days post-colostrom intake, GLSM SVN antibody titers were significantly higher (P ≤ 0.05) in calves from vaccinated dams versus control calves for BHV-1 (T1 = 13.1 and T2 = 17.7)

Beef: Vaccinated dams’ GLSM BVDV2 CVN antibody titers were significantly higher (P ≤ 0.05) for BHV-1 (T1 = 1159.7 and T2 = 1830.7) and PI3 (T1 = 103.1 and T2 = 169.9). Calves from vaccinated dams had post-colostrom antibody titers that were significantly higher than controls (P ≤ 0.05) (T1 = 1159.7 vs. 1231.9, T2 = 1830.7 vs. 2423.9).

INTRODUCTION
Studies have shown that neonatal calves have various levels of immunoglobulins (IgG) following passive antibody transfer from the dam. Variability in neonatal serum IgG levels can be related to the dam’s prior vaccination history, the interval from pre-partum vaccination to parturition, and type of vaccine administered. Strategic vaccination of the dams could improve passive transfer and positively impact neonatal morbidity and mortality. 1.2 3 4

TABLES AND FIGURES (CONT.)

CONCLUSIONS
Modified live vaccination in late gestation cows that were vaccinated pre-breeding with a MLV or KV vaccine, dairy and beef, respectively, resulted in a higher level of serum and colostal antibody titers for multiple viral antigens in dams and their offspring.

REFERENCES
Anamnestic Response

Booster given on day 21
Read the label

• Know the indications and contraindications
  – Species
  – Age
  – Pregnancy
Emerging Respiratory Pathogen

Bibersteinia (Pasteurella) trehalosi
  – Closely related to Mannheimia hemolytic
    • Most labs report out a M. hemolytica on culture results
    • Has leukotoxin, endotoxin and capsular polysaccharide and as a virulence factor
• Has been shown to be resistant to florfenicol
• Until now has been primarily associated with septicemia and systemic pasteurellosis in young sheep and goats
• Similar predisposing factors to M. hemolytica
• Tonsilar crypt colonization?
• More contagious?

**HISTORY**

_Pasteurella haemolytica_

- **Biotype A**: 1959
- **Biotype T**: 1990

- **Mannheimia haemolytica**: 1999
- **Mannheimia glucosida**: 1999
- **Pasteurella trehalosi**: 1990

Recent Name Change

**Bibersteinia trehalosi**
- Ernst L. Biberstein- early pioneer of *P. haemolytica* biotyping

2007

Does this genetically determined genus differentiation manifest itself:
- Clinically?
- Pathogenically?
- Antigenically?
- Response to therapy?

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4 Blackall et. al., *Int. J. Sys. Evo. Microbiology*, 57, 666-
Laboratory Differentiation

- Just one more step and a backup

<table>
<thead>
<tr>
<th><strong>Mannheimia haemolytica</strong></th>
<th><strong>Pasteurella trehalosi</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Trehalose = negative</td>
<td>Trehalose = positive</td>
</tr>
<tr>
<td>Catalase = positive</td>
<td>Catalase = negative</td>
</tr>
</tbody>
</table>

*Ellen Portis, PAH, VMRD, Kalamazoo, MI*
• 30% of state subsidized laboratories are not routinely differentiating
• Reduced by more than half from 2005-2006
• Likelihood rises with increasing dairy population
• Incidence highly variable

* Informal Phone Survey
Conducted by: L.B. Harper, DVM, PAH, Veterinary Operations
Clinical Signs

• First seen in dairy calves in CA, then adult cattle
• Peracute to Acute non responsive pneumonia high death loss and appears to spread (in sheep death within 6-8 hours)
• Primarily seen in start up, expansion or overcrowded dairies
• *Bibersteinia trehalosi* was isolated from several respiratory disease cases in both adult cattle and calves. Often a fibrinous bronchopneumonia with pleuritis has been reported. It has been isolated both in puregrowth and in mixed growth. In one case from this quarter a three-year old Holstein Friesian cow that had been calved ten days showed a severe fibrinous bronchopneumonia affecting all lung lobes with fibrin tags on the visceral pleura. *B. trehalosi* was cultured from lung, spleen, mammary gland and uterine contents.¹

¹ GB surveillance cattle diseases, FIRST QUARTER Date: January – March 2009
Questions?

Hwy 30, traveling to London, KY
Thank you!
Dubovi, E.J., Grohn, Y.T. et al. Response to modified live and killed multivalent viral vaccine in regularly vaccinated, fresh dairy cows 2000 *Veterinary Therapeutics* vol.1, num.1

- Small numbers
- Cows were given Saline, Pyramid or Triangle pre-breeding

"Cows receiving the MLV vaccine were nearly twice as likely to conceive as cows receiving saline. There was no significant difference in the rate of conception between cows receiving the killed vaccine and cows receiving saline."