Applied Reproductive Strategies in Beef Cattle
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Impact of Vaccine Choice on Immunity and Abortion Risk

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Disclaimer

- No interest in or compensation from any pharmaceutical company
- No direct involvement of any pharmaceutical company in preparation of this presentation
- Not a virologist of vaccine expert

Proceedings

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Objective

- Briefly review the impacts of viral vaccine vaccine choice on immunity and abortion risk based on available peer reviewed literature
  - Focused review on literature from the last 15 years
  - Attempted to focus primarily on research utilizing products that are currently available on the commercial market

Abbreviations

- MLV - Modified live virus vaccine
- KV - Inactivated vaccine
- BHV-1 - Bovine Herpes Virus-1
- BVDV - Bovine Viral Diarrhea Virus
- Lepto - Leptospirosis
- PI - Persistent infection with BVDV
- FTAI- Fixed-time Artificial insemination

Are Reproductive Vaccines Needed

- Aono FH et al. *Theriogenology* 79 (2) 2013
  - 4 experiments involving 12,724 beef cows from numerous ranches in Brazil
  - Examined effects of vaccination against BHV-1, BVDV and Lepto and vaccine timing on pregnancy rate and pregnancy loss following FTAI
  - *Vaccination reduced pregnancy loss compared to no vaccination*
  - *Vaccination reduced pregnancy loss in primiparous cows compared to no vaccination or Lepto vaccination alone*
  - *Administering 2 doses of vaccine prior to FTAI improved pregnancy rate compared to vaccination before and after FTAI*

Are Reproductive Vaccines Needed

- Pereira MHC et al. *Animal Repro Science* 137 (3/4) 2013
  - 4 experiments involving 3,640 lactating dairy cattle submitted for FTAI from numerous operations in Brazil
  - Examined effects of vaccination against BHV-1, BVDV and Lepto and vaccine timing on pregnancy rate and pregnancy loss following FTAI
  - *Vaccination reduced pregnancy loss compared to no vaccination*
  - *Vaccination prior to FTAI improved pregnancy rates compared to no vaccination*

Are Reproductive Vaccines Needed

- Results of multiple challenge trials
  - Including challenge by natural exposure
  - Significant difference in vaccinate vs non-vaccinated controls regardless of vaccine used
  - Solid evidence that reproductive vaccination can improve reproductive performance

Vaccine Choice

- **MLV** vs **KV**
  - MLV vaccines
    - Quicker, more robust, longer lasting immune response?
    - Booster not necessarily required
  - KV vaccines
    - Safer than MLV vaccines?
    - Require booster upon initial administration

What's the evidence?

Vaccine Choice

- Direct comparison of MLV and KV vaccines within the same publication is rare
  - Rodning SP et al. *Theriogenology* (73) 8 2010
    - Compared 3 commercial vaccines for protection against natural exposure to PI cattle
      - Vaccinated at 7m, 28 days later, 12 m, and 28 days later
    - Unvaccinated controls
    - **Bovishield GOLD FP5**
    - **Pyramid 5**
    - **Virashield 6**

Vaccine Choice

Rodning SP et al. *Theriogenology* (73) 8 2010

- Viremia in heifers
  - Controls 10/10
  - Bovishield $0/20^{ab}$
  - Pyramid $1/20^{ab}$
  - Virashield $10/20^{a}$
- PI calves
  - Controls 10/10
  - Bovishield $0/19^{ab}$
  - Pyramid $0/18^{ab}$
  - Virashield $2/18^{a}$

Vaccine Choice

- **MLV** vs **KV**
  - Compare vaccine labels
    - Prevention of infection
    - Prevention of disease
    - Aid in disease prevention
    - Aid in disease control

Compendium of Veterinary Products

http://bayerall.naccvp.com/prodindex/main

Vaccine Timing

- Prebreeding vs During Pregnancy
  - Prebreeding
    - Optimizes immunity during period of highest risk
    - Eliminates concern of abortions caused by vaccine
    - May require additional handling
  - During Pregnancy
    - Minimizes additional animal handling
    - May miss period of highest disease risk
    - Risk of abortion?
    - Enhanced colostral immunity?

Efficacy of BHV-1 Vaccines

- Zimmerman AD et al. *JAVMA* 231 (9) 2007
  - **Virashield 6** or sham vaccine, 2 doses prebreeding
  - IV BHV-1 challenge at 180 days of gestation
  - *Virashield 6 – 3/21 aborted*
  - *Controls – 14/14 aborted*

  } *Vaccine provided 87.5% protection*
- Zimmerman AD et al. *Bovine Practitioner* 47 (2) 2013
  - **Express FP 5-VL5** followed by IV BHV-1 challenge
    - Group 1 – 13 months prior to challenge
    - Group 2 – 8 months prior to challenge
    - Group 3 – placebo at both times
  - *Abortions*
    - *Group 1 – 1/7 (7.7%)[a]*
    - *Group 2 – 3/19 (15.8%)[a]*
    - *Group 3 – 18/19 (94.7%)*

Efficacy of BHV-1 Vaccines

- Givens MD et al. *JAVMA* 241 (4) 2012
  - **Express FP 5** – 2 doses prebreeding or sham vaccination
  - Exposed to PI steers for 56 days starting at 45-68 days of gestation
  - Exposed to BHV-1 infected bulls for 14 days starting at 181-204 days of gestation
  - *Abortion*
    - *Vaccinates – 0/22*
    - *Control – 4/10*
  - *PI BVD*
    - *Vaccinates – 0/19*
    - *Control – 10/10*

Efficacy of BVDV Vaccines

- Grooms DL et al. *AJVR* 68 (12) 2007
  - **Cattlemaster GOLD FP 5L5** – 2 doses prebreeding or placebo
  - Exposed to PI cows between 52 and 150 days of gestation
  - Fetuses harvested at approximately 150 of gestation via C-section
  - PI BVD
    - Vaccinates – 4/15 (26.7%)
    - Controls – 14/14 (100%)

Efficacy of BVDV Vaccines

- Leyh RD et al. *AJVR* 72 (3) 2011
  - **Bovishield GOLD FP 5 VL5 HB** once prebreeding or placebo
    - Vaccine contains BVDV 1a and BVDV 2a
  - Exposed to 8 PI cattle for 14 days starting at 64-89 days of gestation
    - BVDV 1b
  - Fetuses harvested at 148-173 days of gestation
  - PI BVDV
    - Vaccinates – 6/40
    - Controls – 8/8

Efficacy of BVDV Vaccines

- Ficken MD et al. *Vet Ther* 7 (3) 2006
  - **Bovishield GOLD FP 5 VL5** or placebo
  - Intranasal challenge 370 days post vaccination with BVDV 1 or BVDV 2
    - 60-90 days of gestation at challenge
  - *PI BVD*
    - *BVDV 1 vaccinates – 0/20*
    - *BVDV 1 controls – 8/9*
    - *BVDV 2 vaccinates – 0/19*
    - *BVDV 2 controls – 10/10*

Efficacy of BVDV Vaccines

- Rodning SP et al. *Theriogenology* (73) 8 2010
  - **Bovishield GOLD FP 5, Pyramid 5, Virashield 6**, or placebo – 4 x prebreeding
  - Exposed to 3 PI animals from 68-126 days post AI
  - PI BVD
    - Controls – 10/10
    - Bovishield GOLD FP 5 – 0/19[ab]
    - Pyramid 5 – 0/18[ab]
    - Virashield 6 – 2/18[a]

MLV Vaccine Safety – Prebreeding

- Effects of BHV-1 on ovarian function
  - Smith PC et al. *AJVR* 51 (7) 1990
    - IV inoculation of MLV BHV-1 vaccine at estrus
    - Evidence of necrotic oophoritis and virus isolated from ovaries of vaccinated heifers
  - Grooms DL et al. *JVDI* 10 (2) 1998
    - 6 heifers and 4 seronegative cows vaccinated with MLV vaccine
    - Heifer ovaries harvested at 8, 10, 12 days post vaccination
    - Cow ovaries harvested at 7, 10, 20, 30 days post vaccination
    - *BVD isolated from ovaries of 3 heifers on day 8, 10 and 12*
    - *BVD isolated form ovary of one cow on day 10*
    - *BVD antigen found in all cow ovaries on day 10, 20 , 30*
    - *Significance unknown*

MLV Vaccine Safety – Prebreeding

- Administration according to label (28 days prebreeding)
  - Numerous studies demonstrate safety and efficacy
- Concern is extra-label use
  - Vaccination too close to breeding

MLV Vaccine Safety – Prebreeding

- Perry GA et al. *Theriogenology* 79 (1) 2013
  - 59 heifers seronegative for BHV-1, BVDV 1 and BVDV 2
  - Group 1 – **Virashield 6 VL5 HB** days 36 and 8 prebreeding
  - Group 2- **Virashield 6 VL5 HB** on day 8 prebreeding
  - Group 3 – **Bovishield GOLD FP 5 VL5** on day 8 prebreeding
  - Group 4 – Saline on days 36 and 8 prebreeding
  - *Pregnancy rate*
    - *Group 1 – 19/21[a]*
    - *Group 2 – 6/7[ab]*
    - *Group 3 – 10/21[b]*
    - *Group 4 – 9/10[a]*
  - *Abnormal Estrus Cycle*
    - *Group 1 – 2/21[a]*
    - *Group 2 – 1/7[ab]*
    - *Group 3 – 8/21[b]*
    - *Group 4 – 0/10[a]*

MLV Vaccine Safety – Prebreeding

- Bolton M et al. Vet Ther 8 (3) 2007
  - 799 heifers with history of MLV vaccine
  - All received **Vista 5 L5 SQ** at 90 ± 25 days prebreeding
  - Controls (n=399) – **Vista 5 L5 SQ** 40 ± 5 prebreeding
  - Test group (n=400) - **Vista 5 L5 SQ** 3 days prebreeding
  - All bred AI based on observed estrus
  - *Conception Rate*

	1st Service	2nd Service	Overall
Controls	67.1%	69.7%	85.1%
Test Group	69.2%	76.2%	86.4%

No differences between groups

MLV Vaccine Safety – Prebreeding

- Walz P et al. *(Presented in abstract form at 2014 ACVIM Forum, Nashville, TN)*
  - Vaccinates (All received initial dose of Express FP 5)
    - Group A - revaccinated Express FP5 10 days prior to synchronized natural breeding
    - Group B - revaccinated Express FP5 31 days prior to synchronized natural breeding
  - Controls (All received initial dose of Citadel VL5)
    - Group C - revaccinated Citadel VL5 10 days prior to synchronized natural breeding
    - Group D - revaccinated Citadel VL5 10 days prior to synchronized natural breeding
  - *No difference in:*
    - *Duration of interestrus intervals*
    - *Proportion exhibiting estrus within 5 days of synchronization*
    - *Serum P4 concentrations*
    - *Pregnancy rates*
    - *Pregnancies within the first 5 days of the breeding season*

MLV Vaccine Safety – Pregnancy

- Sprott LR et al. Bovine Practitioner 35 (2) 2001
  - Pregnant heifers vaccinated with **Cattlemaster 4** preweaning and weaning
  - Group 1 – **Cattlemaster 4** at pregnancy check
  - Group 2 – **Fusion 4** at pregnancy check
    - Contains MLV and KV BHV-1, MLV PI3, and KV BRSV, BVD
  - Group 3 - No vaccine at pregnancy check
  - *One abortion occurred within each group with 56 days post vaccination*
    - *No serology performed*

MLV Vaccine Safety – Pregnancy

- Ellsworth M et al. *Vet Ther* 4 (2) 2003
  - Safety study
  - Bovishield FP 4 L5 prebreeding or unvaccinated
  - All received MLV BHV-1 and BVDV at pregnancy check (160-220 days of gestation)
  - *BHV-1*
    - *6/11 seronegative controls aborted*
    - *0/59 vaccinated heifers aborted*
  - *BVDV*
    - *13 seronegative controls delivered live healthy calves (9/12 calves had prenursing antibody to BVDV 1 and BVDV 2)*
    - *All 59 vaccinated calves delivered live calves (0/58 calves had prenursing abtibody to BVDV)*

MLV Vaccine Safety – Pregnancy

- Ellsworth M et al. *Vet Ther* 4 (2) 2003
- Field studies (all vaccinated prebreeding with **Bovishield FP4 L5**)
  - Controls – not vacinated during pregnancy
  - Vaccinates – **Bovishield FP 4 L5** during pregnancy
  - 1st Trimester (599 beef cows)
  - 2nd Trimester (475 Holstein heifers)
  - 3rd Trimester (348 beef cows)
  - No difference in abortion rate between groups in any study

MLV Vaccine Safety – Pregnancy

- O'Toole D et al. *JAVMA (Pathology in Practice)* 241 (2) 2012
  - Case Report
    - Abortion oubreak in heifers of university owned herd after vaccination with Bovishield GOLD 5 during late pregnancy
    - Heifers had received MLV vaccines on three occasions prior breeding
    - 25% of heifers aborted starting 32 days post vaccination
    - BHV-1 was identified in the aborted fetuses
    - Unable to determine if isolated virus was the same as vaccine virus
    - Demonstrates a temporal relationship but not necessarily cause and effect

MLV Vaccine Safety – Pregnancy

- Gould S et al. *JVDI* 25 (2) 2013
  - Survey of 5 veterinary diagnostic labs from 2000-2011
  - 19, 459 bovine abortions
  - 6,948 tested for BHV-1
  - 264 positive for BHV-1
  - Unable to determine a correlation between BHV-1 positive submissions and history of recent vaccination based on information provided on lab submittal forms
    - BHV-1 negative cases were more likely to have a history of vaccination than positive submissions

Conclusions

- Both MLV and KV vaccines can be efficacious when used according to the label
  - The appropriateness of each type of product will depend on factors unique to each individual operation
- When used according to the label, MLV vaccines are appear to be generally safe whether used prebreeding or during pregnancy at this time
- If MLV vaccines are used in an extra-label manner, evidence exists that adverse reproductive effects are possible
- More research is needed to determine the effects of administering MLV vaccines close to breeding in previously vaccinated cattle

Questions