Intranasal Vaccines in Beef Calves: An Opportunity to Improve Immunity at Weaning

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Overview

- The bovine respiratory disease (BRD) challenge
- Maternal antibody and vaccine interference
- Immune development in young calves
- Response of young calves to intranasal vaccines
- Duration of immunity following vaccination at branding
- Integrating vaccines with management practices
The BRD Challenge

- BRD is a complex with multiple viral and bacterial pathogens interacting in many ways.

- Weaning and transportation of 4-600 lb beef calves creates a population at “high-risk” for BRD and these stressors can double the risk of fatal BRD (Hodgson et al. 2012)

- Metaphylactic antibiotics and vaccination on arrival in the feedlot reduce but do not eliminate the risk of BRD

- An increasing prevalence of antibiotic resistance is restricting the utility of available antibiotics

- Can we develop better vaccination strategies to increase BRD protection at weaning and decrease our reliance on antibiotics?
Barriers to Vaccinating Young Calves

- No evidence of an immune response when a modified-live viral (MLV) vaccine was given intramuscularly (IM) to young calves with high levels of maternal antibody (Ellis et al. 2001)

- Neutralization of MLV vaccine by maternal antibody did not prevent the induction of some immune memory but not known how long this memory lasts (Endsley et al. 2004)

- Calves can respond to a killed bacterial vaccine given IM but failed to induce protective immunity (Chattha et al. 2009; Pihlgren et al. 2004)

- Can maternal antibody interference with MLV be avoided by using an intranasal route of vaccine delivery?
Transfer of Maternal Antibody

- Maternal antibody (90% IgG1; 10% IgA) absorption is optimal during the first 6 h after birth

- Maternal IgG1 persists in blood for months but maternal IgA is cleared in 3-5 days

Hill et al. JAVMA 2012
Maternal Antibody at Branding Time

- Saskatchewan beef herd boosted annually with a pre-breeding MLV vaccine (BVD, IBR, BRSV, PI3)
- 90 calves bled while branding April-May born calves on June 03, 2013
- Very few calves lacked maternal antibody to the 5 viruses used in the pre-breeding vaccine
- Maternal antibody could interfere with an IM MLV vaccine in 95% of the calves
Targeting the Neonatal Mucosal Immune System: Respiratory Pathogens and Intranasal Vaccination.
Newborn Calf Response to Intranasal Vaccination

- Newborn calves fed colostrum from cows immunized with multivalent MLV vaccine (BHV-1, BVDV1, BVDV2, PI3, BRSV)

- Three groups (n = 7) of calves:
  A) No vaccine (naïve controls)
  B) IN vaccination between 3-8 days of age (single vaccination)
  C) IN vaccination between 3-8 days and 35 days of age (booster)

- Monitor vaccine specific IgA antibody levels in nasal secretions
IgA Production Following IN Vaccination

- Maternal IgA cleared from nasal secretions within 3 to 5 days after vaccination
- Increased IgA levels in nasal secretions 10-14 days following IN vaccination
- Endogenous IgA doesn’t block immune response following second immunization at 5 weeks
- Decay of IgA production within one month after vaccination
- Does immune memory persist until weaning?

Hill et al. JAVMA, 2012
Optimal Strategy to Induce Immune Memory IFOMA

Intramuscular versus Intranasal

(Hill et al. Manuscript in Preparation)
Immune Memory in Newborn Calves: IN Versus IM Vaccination

**First Vaccination (3-6 weeks)**

- **Group A** (Diluent)
- **Group B** (IM-Bovishield (MLV))
- **Group C** (IM-Bovishield (MLV))
- **Group D** (IN-Nasalgen-IP (MLV))
- **Group E** (IM-Virashield (KV))
- **Group F** (IM-Virashield (KV))

**Second Vaccination (5-6 months)**

- **Group A** (Diluent)
- **Group B** (Diluent)
- **Group C** (IM-Bovishield (MLV))
- **Group D** (IN-Nasalgen-IP (MLV))
- **Group E** (Diluent)
- **Group F** (IM-Virashield (KV))

**Timeline**

- **June 16, 2014**: Branding: 3-6 weeks old Angus-cross calves
- **October 08, 2014**: Collect serum Select seronegative calves (n = 10/group)
- **October 16, 2014**: Wean/transport Vaccinate
- **October 20, 2014**: BHV-1 challenge

**Controls**

- Bovishield
- Bovishield
- Nasalgen
- Virashield
- Virashield

**BH1 antibody titre**

- Controls: a
- Bovishield: a
- Nasalgen: a
- Virashield: a

**Legend**

- a
- b
Prevention of Clinical Disease: Following Primary Immunization IFOMA and Booster at Weaning

![Graph showing BHV-1 shedding post-challenge](chart.png)

- **Naive Controls**
- **Once Bovishield (MLV IM vaccine at branding)**
- **Twice Bovishield (MLV IM vaccine boosted at weaning)**
- **Twice Nasalgen-IP (MLV IN vaccine boosted at weaning)**
- **Once Virashield (KV IM vaccine at branding)**
- **Twice Virashield (KV IM vaccine boosted at weaning)**
Conclusions

- IN vaccination at branding was the only strategy to induce immune memory that was able to prevent viral infection when a secondary IN vaccination was given the day after weaning.

- IM MLV vaccine at branding did not provide sufficient immune memory to prevent viral infection when a secondary IM vaccination was given the day after weaning.

- IM KV vaccine at branding also failed to reduce viral shedding when a secondary IM vaccination was given the day after weaning.

- IN vaccination at 3 to 6 weeks combined with a booster at 5 to 6 months provides a strategy that protects both individual animals and limit disease transmission (herd immunity).
Integrating Management and Vaccination

- Branding provides an opportunity to deliver MLV vaccines to young calves but the vaccine delivery route used should consider the vaccination program used for the cows.

- MLV vaccines given IM at branding time, when maternal antibody is present, provides no benefit when giving a second IM vaccination at weaning.

- MLV vaccines given IM three weeks pre-weaning (pre-conditioning) when maternal antibody has waned provides good protection at the time of weaning.

- MLV vaccines given IN at branding avoids maternal antibody interference and provides immune memory that can be rapidly boosted by a second IN, but not IM, vaccination the day after weaning.
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Nasaopharyngeal Tonsil in Newborn Calves

Fetus

Day 21

GC

IgA

Epithelial Surface

slgA

PCs