Vaccinating the Dairy Heifer and Cow: What Approaches Work?

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Topics
- Activating the Immune Response-
- Heifer Vaccination
- Prepartum vs Postpartum Cow Vaccination

Credits
- Kuby Immunology
- Immunobiology, 6th edition
- David Topham, University of Rochester

Immune responses

Inflammatory Response

A proper vaccine response will result in chemotaxis

What Does Stress or BVD Do to chemotaxis?
Inflammatory Response
What Does Stress or BVD Do for Neutrophil Response?

Neonates-4X neutrophils, ↓chemotaxis and killing
Neutrophil Chemotaxis and Phagocytosis

The host immune response to infection

Timing and the Adaptive Immune Response-Anamnestic Response

Heifer Development
- Reproductive Disease- IBR, BVD and Lepto (Neospora)
  - MLV-1-2 dose
    - >6 months and 2 months before breeding
  - Inactivated-2 doses Viral-Lepto 5 weeks and 2 weeks before breeding
- Enteric Disease Vaccines
  - Adjuvanted-give sooner, last longer
  - Non-adjuvanted- give closer to calving
- NCP BVDV- it is the virus that causes PI-traffics different not just about epitopes
Why Vaccinate Heifers with NCP BVDV?

<table>
<thead>
<tr>
<th></th>
<th>Non-Cytopathic (NCP)</th>
<th>Cytopathic (CP)</th>
</tr>
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<tbody>
<tr>
<td>Major Field Isolate</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Mutant Virus</td>
<td></td>
<td>X</td>
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<tr>
<td>Cause of PI Calves</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Present in Mucosal Disease</td>
<td></td>
<td>X X</td>
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<tr>
<td>Virus used in most vaccines</td>
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<td>X</td>
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</tbody>
</table>

NCP Studies

- Vaccine Studies Protected against BVDV 1a, 1b, & 2a challenge in 3 published studies (acute disease and PI)
- Trafficks to mucosal surfaces- tonsil, Peyers patches, mesenteric lymph node- unlike CP

Clinical Forms of BVD

Acute Infection
- Nonpregnant Pregnant Cow
- PI calf 40-150 days
- May die of MD, offspring always PI

Chronic Peracute Mild Fetus-Infected Fetal Death PI calf 40-150 days Normal

BVDV is shed lifetime
- BVDV is shed 1-14 days up to 60 days

BVDV Vaccination-Fetal Protection

- Prior to breeding
- Heifer development program - Need to use a NCP BVDV vaccine
- No evidence of protection the following year from cows vaccinated during pregnancy- Challenge studies

NCP BVDV Vaccines- Cons

- Can't use them in pregnant animals
- In bulls- Testicular persistence- NO- PCR- no replicating virus semen does not cause any seroconversion in inseminated heifers

Herd Vaccination Program- IBR Precautions

- Prematuration
  - Heifers- Naive
    - MLV-Corpus Luteum- US-Northernavax 2 months before breeding
    - MLV-Pre-existing immunity-No effect
  - Cow Herd
    - MLV-Pre-existing immunity-No effect
IBR Reproductive Disease

- Localized Infections
  - Vulvovaginitis
  - Balanoposthitis
- Reproductive Failure
  - Infertility-CL
  - Inflammation-Necrosis
  - Abortion, Early Embryonic Death

Clinical Forms of BHV-1

- Acute Infection
  - Respiratory/Reproductive
  - IBR is shed 2-10 days
- Latent/Reactivated
  - Abortion 2 wks-2 mos
  - IBR is shed 2-10 days
  - Lab can Reactivate

BHV-1 (IBR) Abortion

- Incidence decreased dramatically in last 30-40 years due to vaccination (prior to pregnant cow claim)
  - SDSU
    - 1968-72: 16% of all positive diagnosis
    - 1979-89: 5.4% of all positive diagnosis
- Most abortions occur after 4 months of gestation
- Fetuses typically retained 48-72 hours
  - Autolysis makes laboratory diagnosis difficult
- Can affect 1% to over 50% of herd

BHV-1 Abortions Diagnosis at SDSU

- From 1991-2005 number of BHV-1 abortions diagnosed was 1-10/year. Some cases were due to the administration of BHV-1 MLV abortions.
- In 2005-2006 there were 17 BHV-1 abortions and 11 had histories that BHV-1 MLV vaccines had been administered 2-4 weeks before the onset of the BHV-1 abortions

Summary

- BHV-1 vaccination prior to breeding has resulted in decrease in incidence of the disease
- BHV-1 abortions characterized by long incubation period
- Use of BHV-1 vaccines in gestation has increased the number of BHV-1 abortions
Vaccines & Cows

- How many of the vaccine licensing claims were done in dairy cows?
  - None

- Duration of Immunity
- Safe in Pregnant Cows
- PI Studies

Prepartum (Pregnant) Cow

Vaccinating Prepartum Cow

- Two targets
  - Cow
    - Reproductive Diseases-Cow- Lepto, IBR, BVDV, Neospora
    - Mastitis-Colibacillus
  - Calves- Colostrum
    - Respiratory Disease IBR, BRSV, PI3, BVDV?
    - Enteric Diseases-E. coli, Clostridial, Rotaviruses, Coronavirus, BVDV?

IgG Transport

- Although IgG begins moving to mammary gland at 4-6 weeks, big push begins at 2 weeks prior to calving (window of opportunity)
- Important high sustained serum Ig levels throughout calving
- Serum Ab levels directly correlate with maternal Ab levels
- Oil adjuvanted products provides sustained Ig levels

Colostrum Ig Concentration

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<tr>
<th>Immunoglobulin</th>
<th>Serum</th>
<th>Colostrum</th>
<th>Milk</th>
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<tr>
<td>IgG-total (mg/ml)</td>
<td>75.0</td>
<td>32-712</td>
<td>0.72</td>
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<tr>
<td>IgG1</td>
<td>14.0</td>
<td>20-200</td>
<td>0.6</td>
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<tr>
<td>IgG2</td>
<td>11.0</td>
<td>12.0</td>
<td>0.12</td>
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</table>

* IgG, IgM, and IgA of total Ig in serum, colostrum and milk (from Laser, 1997).
Prepartum (Pregnant) Cow

Physiological Challenges
- Pregnancy
- Pre-existing Immunity

Immunosuppression and the pregnant cow
- Placenta and Uterine cytokines (local effect)
- Progesterone
- Estrogen (at the end of gestation)
- Cortisol (at the end of gestation and carries over into early postpartum period)
- Bovine Pregnancy Associated Glycoprotein (late prepartum)

Maternal Immune Suppression
- \( \uparrow \) PGE2
- \( \uparrow \) IL-4
- \( \uparrow \) IL-10

The cow's immune system must be immunosuppressed to prevent rejection of the calf.

The pregnant dairy cow and the immune response
- The pregnant cow
  - The pregnant cow is immunosuppressed
  - Longer stimulation - necessary for sustained immune response

MLV vs Inactivated Vaccine

Vulnerability to Antibody
- Size of Antigenic Mass
- Antigenic Agent
- Type of Adjuvant used in the Vaccine

Humoral Effector Mechanisms against Viruses

Neutralization
- Virus uncoating blocked
- Precludes infection
- Prevents viral gene expression
Size of Antigenic Mass

- Conventional injectable MLV vaccine in the presence of humoral antibody
- Small antigenic mass
- Vaccine virus is neutralized by antibody
- Vaccine virus fails to reach and infect animal cells
- Vaccine virus fails to replicate
- Vaccine virus fails to stimulate immune response

Pregnant Cows and MLV Vaccination

What was the origin of safe in Pregnant Cows Claim?

- Companies requested safe for use in calves nursing pregnant cows (Beef Claim)
- USDA decided that it would extend the claim to safe in pregnant cows
  - Animals vaccinated with the same product within 12 months
- Pregnant cow claim is only a safety claim. There is no efficacy data indicating that vaccination during pregnancy had any effect on reproductive health in subsequent pregnancy
- Twelve month duration of safety

Safety and Animal Herpesvirus Vaccines

- Well documented that IBR MLV vaccines are abortifacient agents
  - First reported 1968- various reports since in naïve and animals with unknown vaccination history
  - IBR destroys the corpus luteum- as effective as prostaglandins
- Safety=Efficacy??? Confusion remains supreme

Misuse- Opening Pandora’s Box

- Safe in pregnant animals vaccinated with the same product prior to breeding (within 12 months)

Duration of Safety Claim Vaccination

- Safe in pregnant animals vaccinated with the same product prior to breeding (within 12 months)
Cow Vaccination Schedule - SDSU Dairy

Population Distribution - Susceptibility

Summary

- Pregnant dairy cows have two targets:
- Pregnant cows are immunosuppressed
- Pregnant cow claim - Safety, not efficacy
- In a population of beef heifers, abortion rate <1:1000

Vaccinating the Postpartum Dairy Cow

Postpartum Dairy Cow

- Postpartum immunosuppression
- Lose the opportunity to boost colostrum
- Pre-existing Immunity - Interference
- Energy Drain
- Ketosis and acidosis - immunosuppression
Immunosuppression and Postpartum Cow
- Estrogen
- Cortisol (at the end of gestation and carries over into early postpartum period ~ 1 week)
- Bovine Pregnancy Associated Glycoprotein (late prepartum and carries over into early postpartum period ~ 1 week)
- Ketoacidosis

Immunosuppression and Calving

Innate Immunity

Acquired Immunity

Immunity and Energy
- Immune system doesn’t get a free ride- energy consumer
- Multiple demands on energy for the postpartum cow

Young Dairy Heifer

Breeding Heifer
The role of acidogenic diets and beta-hydroxybutyrate on lymphocyte proliferation and serum antibody response against bovine respiratory viruses in Holstein steers

DC Donvan, AR Hippen, DJ Hurley, CCL Chase

J Anim Sci 2003; 3088-3094

Material & Methods

Latin Square Design

Table 1: Composition of basal and treatment diets

<table>
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<tr>
<th>Ingredient</th>
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<td>acidified</td>
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<tr>
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<tr>
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<tr>
<td>Methionine</td>
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</table>

Four month old steer calves

Vaccinated with 2 doses of killed 4 way viral vaccine
Body Condition and Immune Response

- Eight Holstein dairy cows
- Body condition scores at 14 d prepartum
- Blood samples and liver biopsy were taken weekly at −14, 7, 0, 7, 14, 21 d postpartum
- Tested Blood samples:
  - Ketones - BHBA and NEFA concentrations
  - BRSV Antibodies
  - BRSV Cell Mediated Response

Correlation between prepartum body condition score and cell mediated response

Correlation between NEFA and circulating memory activity to BRSV

Correlation between blood NEFA and Serum Neutralization to BRSV
Summary

- Vaccination Programs
  - No data on the effect of vaccinating pregnant animals on reproductive efficiency in subsequent pregnancy
  - Postpartum dairy cow has lots of issues: immunosuppression, acidosis and ketosis
  - When is the best time??

Beef Cows and Vaccination

- Metabolic issues that affect the fresh dairy cow vaccine responses are not important for the beef cow
- Beef cow reproductive vaccines should be given following calving but before breeding
- Scours vaccines are given late in pregnancy