Protecting against Reproductive and Clinical disease in cattle caused by BVDV, BHV1 and BRSV

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Immunology
Bovine Viral Diarrhea (Pestivirus) Disease Overview
Bovine viral diarrhea syndromes are caused by a group of related viruses.
These related viruses may cause severe disease in unprotected animals

- Immune suppression
- Severe diarrhea
- Bleeding problems due to platelet destruction (type 2s only)
- Severe respiratory
- High death loss
BVD Immune Suppression

Results in more severe disease
  – BRD (Bovine Respiratory Disease)
    BRSV
    IBR
    Pasteurella (Mannheimia) haemolytica
  – Salmonella
  – Neospora
  – Calf diarrhea
    • Rotavirus
The majority of BVDV infections are unnoticed (subclinical)

Over 75% of all BVDV infections are subclinical
Often not noticed
In dairy and beef herds will show up as:
  - Reproductive failure
  - Immune suppression in adult animals
  - Calf problems
  - pneumonia
  - scours
Clinical Reproductive Syndromes Associated with BVDV Infection

Fetal Infections
Abortion / Return to Estrus
- 0-40 days
Production of “PI” Calves
- 40-120 days
Fetal anomalies / Weak Calves
- 120-160 days
BVDV PI in Breeding Bulls / infected semen

1. Higher levels of BVDV in semen than in serum
   - Shedding is constant in the semen of PI bulls
   - It is not within the spermatozoa
   - Adverse impact of the infection on sperm quality is debated
   - Primary sites of viral replication are most likely to be prostate gland and seminal vesicles
   - No BVDV antibodies in seminal fluid
Impact of BVDV PI in Breeding Bulls and Infected Semen

1. Relatively low number of PI calves result from the breedings with PI bulls
2. In sero-negative animals dramatic decreases in conception rates and increases early fetal death
3. Uterine infections can occur in both sero-negative and sero-positive animals.
4. Sero-conversion will occur in sero-negative animals after exposure to semen from PI bulls
5. Horizontal and vertical transmission important with PI bulls
Impact of PI in Embryo Transfer

PI donor cows
- have not been shown to cause PI calves to be born
- May cause decreased conception rates
- May be a source of BVDV contamination

PI recipients
- have been shown to cause PI calved to be born
- May cause decreased conception rates
- May be a source of BVDV contamination

Thus both the donor and recipient should be screened for BVDV
BVDV Background
Cytopathic versus Noncytopathic BVDV
Cytopathic versus Noncytopathic BVDV

Noncytopathic BVDV is the natural state of the virus
Cytopathic strains arise from mutation of a noncytopathic strain
It is a laboratory differentiation
It is not related to virulence
Primary importance of the difference is in the reproductive form of BVDV
BVDV Classification

• Genotype
  – 1a
  – 1b
  – 2a
  – 2b?

• Biotype
  – Noncytopathic
  – Cytopathic
Relationships Among the Pestivirus Family...
Persistent Infection

Only occurs following in utero exposure

Virus crosses the placenta before the immune system has developed

Calf learns to recognize the that strain of BVD virus as part of self
Persistent Infection - Routes

Acute infection - pregnant female exposed to NCP
BVDV

Persistently infected calf

Persistently infected female giving birth

93%

7%

Persistently infected Calves

May be born weak and runted

May be born clinically normal

Are immunologically frail

Are persistently infected forever

Are the source of BVDV spread in most herds

May remain in the herd as cows and bulls spreading the virus
Outcomes of Persistently Infected Calves

50% of PI cattle will die within first year of life

Outcomes

- Death at/near time of birth
- Death due to mucosal disease
- Death from other cause but BVD immune compromising was factor
- Survive to maturity but less than healthy
- Survive to maturity and reproduce

(Duffell & Harkness Vet Rec 117:240-245, 1985)
BHV-1

Genetically stable DNA virus
Rapid transmission, primarily aerosol
Immunosuppressive
Trigeminal nerve latency via the latency gene
  – Recrudescence
  – Vaccine latency
Causes intracellular bridges – blocks antibody neutralization, cell mediated immunity very important protective component
Once an animal infected: latent carrier for ever

LATENCY → Persistence of IBR, even in a closed herd

REACTIVATION → REEXCRETION

VIRAL EXCRETION CYCLES

SOME WEEKS TO SOME YEARS BETWEEN CYCLES
Rapid transmission
Bovine herpesvirus 1 Disease Syndromes

Severe respiratory infections
Reproductive losses
Eye and nerve lesions
Venereal form
  – infectious pustular vulvovaginitis in cows
  and infectious balanoposthitis in bulls
Bovine herpesvirus 1 Disease

Syndromes

Respiratory disease (rednose)
- Most recognized syndrome
- Primarily upper respiratory tract and tracheal involvement
  Reddening of nasal passages and nasal discharge
  Anorexia, lethargy, weight loss
  Tracheal damage and pseudomembranes
  Uncomplicated death loss usually less than 5%
  Complicated infections may hit mortality rates of 60%
Bovine herpesvirus 1 Disease Syndromes

Reproductive losses

- Can cause mid to late term abortions
  - Conception failure
  - Early embryonic death loss
  - Follicular and luteal necrosis
    - Does not occur in sero-positive cattle
      - Spire and Cortese
  - Can occur with MLV vaccination
IBR Reproductive Effects

Abortion storms
  – Abortions may be delayed
  – Feti are often autolyzed

Reduced milk production

Reported up to 50% abortion rate in outbreaks
Bovine herpesvirus 1 Disease

Syndromes

Eye and nerve lesions

Keratoconjunctivitis similar to pink eye may be seen

Damage of facial nerves and facial nerve paralysis
Bovine herpesvirus 1 Disease Syndromes

Venereal form

– infectious pustular vulvovaginitis in cows
and infectious balanoposthitis in bulls
Respiratory Syncytial Virus - BRSV

Envelope spikes
- G
- F
- SH

Lipid membrane
- M
- M2

Nucleocapsid
- SS RNA
- N
- P
- L

Non-structural
- NS1
- NS2

Respiratory syncytial virus

http://www.iah.ac.uk/research/BRSV/images/BRSV.jpg
**Bovine Respiratory Syncytial Virus**

- BRSV is an enveloped single stranded RNA pneumovirus in the paramyxovirus family.
- In addition to cattle, sheep and goats can also be infected.
- Respiratory Disease due to BRSV occurs predominantly in young beef and dairy cattle.
- Can be isolated from the respiratory tract of clinically normal cattle.
Bovine Respiratory Syncytial Virus

• BRSV virus is named for its characteristic cytopathic effect— the formation of syncytial cell.
• BRSV is associated with the killing of mucosal cells which results in the formation of giant multinucleated cells (known as syncytia) created by the merging of several cells
BRSV

- Closely related to HRSV
- Can cause severe lower respiratory tract infections in naive cattle
- Can cause severe lower respiratory tract infections in cattle nutritionally compromised
- Can predispose to secondary infections
- Can also cause mild upper respiratory tract
BRSV

• Along with PI3 are the two most common respiratory pathogens for cattle to be exposed to as evidenced by serological surveys
• Spreads very rapidly due to aerosol transmission
• Sero-negative animals will often sero-convert during trailer rides
BRSV is endemic

- Seroprevalence studies in the worldwide indicate 61-81% of cattle are exposed to BRSV\textsuperscript{1,2,3}

Bovine Respiratory Syncytial Virus
BRSV has affinity for respiratory cells

Bovine turbinate cells infected with *Bovine respiratory syncytial virus* revealed by an anti-F antibody 7 days post-infection.

BRSV syndromes include:

- Peracute
- Acute
- Secondary pneumonic
- Mild “cold” form
BRSV

• Severe lower respiratory tract infections
• Mild upper respiratory tract infections
• Nutritional component
• Forms syncytia – blocking neutralizing antibodies
Calves most at risk

• calves are particularly sensitive to BRSV
  – maternal antibodies may not be protective
    • incidence and severity of disease inversely related to level of specific maternal antibodies
  
• older calves and cows can get severe disease as well if naive to the virus or nutritionally challenged

BRSV Vaccination in Dairy Cows

• BRSV vaccination associated with\(^1\):
  – Higher milk production 1.4kg [3.06 lb] more milk/d in first parity cows during the first 21 weeks of lactation
  – Higher conception rates at first insemination:
    • First-parity cows (54.6 vs. 32.7%)
    • Second-parity cows vaccinated With the four-way vaccine (47.8% vs. 28.9)

BRSV in beef calves/cows?

- Lower or no BRSV antibodies in colostrum
  - if they are no vaccinating cows then colostrum low for ALL viruses
- Cows shedding BRSV virus, other viruses?
- Reduced herd immunity
Benefits Vaccination of Dams and Calves for BRSV

- Higher antibodies in colostrum
- Higher herd immunity
- Silent priming of immune system
- Protection through weaning from CMI

1. Ellis JA, Hassard LE, Cortese V, Morley PS: The effect of perinatal vaccination on humoral and cellular immune responses in cows and young calves. JAVMA vol 208 no. 3 1996 pgs 393-400
BRSV and Vaccination

- BRSV vaccines are by nature temperature sensitive
- Following systemic vaccination the virus undergoes limited, aberrant replication
- Virus can not be isolated following vaccination
- Systemic vaccination does not stimulate appreciable amounts of IgA
BRSV and Vaccination
Continued

- Protection is a combination of CMI and Humoral immune responses
- Systemic vaccination will not stop BRSV from infecting lungs
Proteção à altura da sua produtividade.
What’s New?

- New with killed BVD Type 1 and 2
- Manufactured to ensure the critically important BVD viral proteins are at optimal levels
- New, next-generation adjuvant system—PreZent-A
- Beef Friendly™ subcutaneous administration
What Does This Mean?

New killed BVD vaccine—unprecedented claims

- Fetal protection BVD Type 1
- Fetal protection BVD Type 2
- Aids in prevention of IBR abortion
- Outstanding respiratory protection against lethal BVD Type 2 challenge\(^1\)

\(^1\)Data on file, Pfizer Inc
Redefining Killed BVD Protection

Only CattleMaster GOLD offers the safety and flexibility of killed vaccines with superior fetal and respiratory protection.
Breakthrough BVD Fetal Protection

While no vaccine can guarantee 100% efficacy, these studies showed 100% protection from BVD Type 1 and 88% from BVD Type 2 persistent infection when animals were vaccinated according to label directions with CattleMaster GOLD.

Studies Confirm Fetal Protection

- 100% protection for BVD Type 1 calves
- 100% protection for BVD Type 2 calves
- 100% of healthy calves

Non-vaccinate results:
- 100% PI calves, BVD Type 1
- 88% PI calves, BVD Type 2
CattleMaster Gold stimulates very high BVDV SN titers

- Virus Neutralization Titer
- Log2 Form Dilution
- 2:1:4
- 3:1:8
- 4:1:16
- 5:1:32
- 6:1:64
- 7:1:128
- 8:1:256
- 9:1:512
- 10:1:1,024
- 11:1:2,048
- 12:1:4,096
- 13:1:8,192
- 14:1:16,384
- 15:1:32,768
- 16:1:65,536
- 17:1:131,072

**Virus Neutralization by Vaccine Induced Antibody**

**BVDV Strain**

- SC-Resp
- IM-Resp
- SC-Fetal
- IM-Fetal
## Classification of BVD viruses used in viral neutralization

<table>
<thead>
<tr>
<th>Virus</th>
<th>Genotype</th>
<th>Biotype</th>
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<tbody>
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Breakthrough IBR Fetal Protection

New Claim—First & Only for a Killed BVD Vaccine

Aids in the prevention of IBR-induced abortions
## BHV-1 Fetal Protection

Number of animals by treatment and key study event

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Animals</th>
<th>Abortion</th>
<th>Stillborn</th>
<th>Normal Calf</th>
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<td>Vaccinates</td>
<td>13</td>
<td>1</td>
<td>1</td>
<td>11</td>
</tr>
</tbody>
</table>
The First & Only Low Passage BRSV

• PAH Low Passage BRSV:
  – All product produced from Master Seed passed only 8 times

• Competitors BRSV Master Seed*
  – Original isolate passed 7 times in kidney cells
  – Then passed 8 times in bovine turbinate cells
  – Then passed 46 times in bovine kidney cells
  – Working seed passed 4x more in kidney cell

*Bayer Corp. BRSV VAC
How is This Possible?

• Innovative next-generation adjuvant system
• Delivers unprecedented protective levels
• Adjuvant systems like PreZent-A are known to stimulate both cell-mediated and humoral immune responses²

Obrigado!

Proteção à altura da sua produtividade.
Thank You!