Bovine Viral Diarrhea Virus

Alter Ego as a Reproductive Pathogen

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Greetings From Michigan State University
Today’s Objective

- Brief overview of BVDV
- Review of reproductive consequences
- BVDV Control
What is BVDV

- Viral infection of cattle
  - Sheep, pigs, camelids, cervidae
- RNA virus
  - Can rapidly mutate and change (Think “Flue virus”)
- Diverse clinical presentation
- Diverse antigenic make-up
  - Vaccine failure
  - Diagnostic challenges
BVDV Overview

Mucosal Disease

Normal Congenital Defects

"Weak Calf" Syndrome

Abortions

Normal Poor Performance

Immunosuppression

Acute Death

Immunosuppression

Acute Diarrhea

Subclinical Infection

Acute/Transient/Primary Infection

Fetal Infection

CI’s

Abortions

Normal

Congenital Defects

Persistent Infection

“Weak Calf” Syndrome
BVDV and Reproduction

- All aspects of reproduction affected by BVDV
- Both biotypes and all genotypes can cross placenta and infect the fetus
- Clinical outcome depends on:
  - BVDV isolate (biotype, virulence)
  - Stage of gestation
  - Immune status of dam
- Clinical outcome in dam include any associated with acute or transient infection.
  - Subclinical
  - Clinical disease
BVDV: Reproductive Disease

- Infertility
- Early Embryonic Death
- Persistent Infection
- Congenital Defects
- Abortion
- Embryos/IVF
- Bulls
Time line of BVDV effects on Bovine Reproduction

- EED
- Immunotolerance
- Congenital Defects
- Congenital Infections Normal? - Seropositive
- Abortion

Month
Estimated BVDV Related Losses Over 18 Months in Ohio Dairy Farm (Gross Loss)

**Milk Production**
- Decreased Production: $348,521
- Decreased Cow Numbers: 10,457

**Increased Services/Conception**
- Total: 3,010

**Abortions /Still born**
- Female: 14,600
- Male: 7,300

**Death Losses**
- Heifers 0-2 months: 20,000
- Heifers 2-6 months: 3,780
- Heifers 6-24 months: 27,000
- Mature Cows: 23,800

**Veterinary Costs**
- Total: 15,000

**Total**
- $473,468 USD
BVDV and Reproduction

- Transient Infertility
  - Infection around the time of breeding (+/-9d)
  - Reduced conception rate
BVDV and Infertility

McGowan et. al., 1993
BVDV and Reproduction

- **Transient Infertility**
  - Infection around the time of breeding (+/-9d)
  - Reduced conception rate

- **Mechanism unknown**
  - Failure of fertilization
  - Direct effect on early embryo
  - Hostile uterine environment
  - Ovarian dysfunction
    - Oophoritis
    - Changed follicular dynamics
## BVDV and Ovaries

<table>
<thead>
<tr>
<th>Day Post Infection</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
<th>14</th>
<th>16</th>
<th>18</th>
<th>25</th>
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<tbody>
<tr>
<td>Virus Isolation</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>IHC</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Oophoritis</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>+</td>
</tr>
</tbody>
</table>

Grooms et al., 1998
Early embryonic death

- Infection from breeding to day 45 of gestation.
- Direct effect on embryo following hatching from the zona pellucida (day 7)
  - abnormal estrous cycle lengths
  - cows diagnosed pregnant then recycle
  - deceased pregnancy rates
BVDV and Early Embryonic Death

McGowan et al., 1993
BVDV and Reproduction

- Abortion
  - Can occur at any time during gestation.
  - Most common during first 2 trimesters
  - Virus causes death of developing fetus.
  - Fetal expulsion is often delayed for weeks following infection -- diagnostic dilemma.
    - Necrotic fetus
    - Virus gone
    - Dam seroconverts before fetus expelled
Pathogenesis of abortion unknown

- Placentitis w/ or w/o secondary bacterial infection
- Direct effect on replicating cells
- Congenital defects
- Persistent infection
## BVDV Positive Abortions

<table>
<thead>
<tr>
<th>Source</th>
<th>% BVDV Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson et al, 1990</td>
<td>1.5%</td>
</tr>
<tr>
<td>San Joaquin Valley, CA</td>
<td></td>
</tr>
<tr>
<td>Kirkbride, 1992</td>
<td>4.54%</td>
</tr>
<tr>
<td>South Dakota</td>
<td></td>
</tr>
<tr>
<td>Woodard, 1994</td>
<td>27.2%</td>
</tr>
<tr>
<td>Wyoming</td>
<td></td>
</tr>
<tr>
<td>Alves et al, 1996</td>
<td>4.1%</td>
</tr>
<tr>
<td>Ontario, Canada</td>
<td></td>
</tr>
<tr>
<td>Jamaluddin et al, 1996</td>
<td>0.5%</td>
</tr>
<tr>
<td>California</td>
<td></td>
</tr>
<tr>
<td>Yamini, 1995</td>
<td>0.1%</td>
</tr>
<tr>
<td>Michigan</td>
<td></td>
</tr>
<tr>
<td>Murray, 1990</td>
<td>26%</td>
</tr>
<tr>
<td>Southern England</td>
<td></td>
</tr>
</tbody>
</table>
BVDV and Reproduction

- Congenital Defects
  - Result of fetal infection between 100-150th day of gestation.
    - Final stages of organogenesis and the development of immunocompetence.
  - Direct effect of virus on cells
  - Immunocompetence >>> Inflammation >>> Tissue damage
Congenital Defects Associated With BVDV

- Nervous system
  - Cerebellar hypoplasia
  - Microencephalopathy
  - Hydrocephalus
  - Porencephaly
  - Hypomylinogenesis
  - Hydranencephaly

- Eye
  - Retinal atrophy
  - Cataracts
  - Microopthalmia
  - Optic nerve neuritis

- Immune system
  - Thymic hypoplasia

- Skin
  - Hypotrichosis
  - Alopecia

- Musculoskeletal
  - Brachygnathism
  - Growth retardation
  - Arthrogryposis
BVDV and Reproduction

- **Calves born seropositive to BVDV**
  - Occurs when fetal infection occurs after fetal immunocompetence develops (After 125 days).
  - Fetus mounts immune response which clears virus.
  - Will have BVDV neutralizing antibodies at birth.
  - Calf may still develop pathology depending on timing of infection.
    - <180 days -- Congenital defects
    - >180 days -- Normal calf ??
    - Anytime -- Virulent strains -- Abortion
Calves Born Seropositive to BVDV? Are They Normal?

- Munoz-Zanzi et al, 2002
  - Heifers born seropositive to BVDV had 2 fold higher risk of severe morbidity event in first 6 months of life
  - Heifers with evidence of congenital BVDV infection had lower fertility than non-infected heifers (15-42 days longer time-to-first AI)
  - Long term effects??????
BVDV and Reproduction

- **Immunotolerance to BVDV**
- **Also Know as Persistent Infection or PI’s**
  - Occurs following fetal infection prior to 125th day of gestation.
    - Immune system developing.
    - “Subclinical” fetal infection -- fetus survives
    - Virus recognized as a self antigen.
    - No antibodies are produced against the persistent BVDV or homologous virus.
    - Virus allowed to replicate unchallenged.
  - Has **only** been documented with ncpBVDV.
  - Result: Cattle which are immunotolerant and persistently infected with BVDV.
Characteristics of PI’s

- Infected for life
- No treatment
- Shed large amounts of virus in all secretions and excretions
- Major source of virus spread within and between farms
  - Identifying and eliminating PI’s is key component of control program.
Characteristics of PI’s

- PI’s give birth to PI’s
  - Persistent infection that crosses placenta and infects fetus
- Non-PI’s can give birth to PI’s
  - Transient infection that crosses placenta and infects fetus
Just call me typhoid Bubba!
Bulls

- BVDV can be isolated from:
  - Semen of acutely and persistently infected bulls
  - Raw, extended, and frozen semen
- Virus can be spread via semen to susceptible females/farms.
Embryos

- Embryo’s by themselves are not a large risk of BVDV transmission if collected properly
  - Methods outlined by International Embryo Transfer Society (IETS)
- But……recipients are another story…….
An Integrated Approach To Controlling BVDV in Cattle Operations
Goals

- BVDV control starts with understanding goals of the operation
  - Control programs may be much different for a commercial dairy operation compared to a purebred beef seed-stock operation.
Risk Tolerance

- Different levels of risk tolerance
  - Risk adverse may have more stringent control program
  - Risk tolerant may be willing to accept certain levels of “BVDV risk”, therefore a less stringent BVDV control program
Risk Assessment

- Risk of BVDV transmission between and within herds varies
  - Closed diary herd at less at risk than a commercial beef herd that purchases 50 pregnant replacement heifers annually from unknown backgrounds
BVDV Control Tools

Diagnostic Assays/Strategies

Vaccines

Biosecurity Measures
BVDV Control Tools

- Diagnostic Assays/Strategies
- Vaccines
- Biosecurity Measures
Ohio Dairy
March 95-May 96

Number of Abortions

Month of gestation

BVDV NEG
BVDV POS
Sources of BVDV Exposure

- **PI’s or Transient Infections**
  - Replacements
  - Exhibition
  - Fence line
  - Shared pastures
  - Semen
  - Embryo’s/Recips

- **Other Species**
  - Sheep/goats
  - Camelids
  - Cervidae
  - Insects

- **Inanimate Fomites**
  - Vehicles
  - Equipment
  - People
BVDV Control Tools

- Diagnostic Assays/Strategies
- Vaccines
- Biosecurity Measures
MOST WANTED

Known carrier of a virulent virus...Persistently infected with BVDV

CONSIDERED ARMED AND EXTREMELY DANGEROUS

IF YOU HAVE ANY INFORMATION CONCERNING THIS PERSON, PLEASE CONTACT YOUR VETERINARIAN

REWARD

“Seek and Destroy” PI Cattle
Detection of PI’s

Tests To Detect PI’s

- Virus Isolation IPMA
- Skin IHC/FA/ELISA
- PCR Individual/Pooled
- Blood ELISA

SEROLOGY X
Herd Screening Tests

Serology on Sentinels
- Unvaccinated calves 6-12 months
- Target cohorts
- Both Type 1 and 2

Bulk Tank PCR
- Looks only at lactating cows
- 300 cows pools

Pooled PCR
- Groups of 10-100
- Cost effectiveness lost when prevalence of PI’s is >10%

Negative
Continue Herd Screening

Positive
Individual Testing
Test all Calves and Adults w/o offspring
Assumption: Calves most likely to be PI’s
Calves serve as sentinels for dams

Pooled PCR
- Positive
  - Individual Test
  - Options: Isolate and Retest Eliminate

Skin IHC or ELISA
- Positive
- Negative
  - If Calf
    - Options: Isolate and Retest Eliminate

VI/IPMA
- Positive
- Negative
  - If Calf
    - Test Dams
      - Positive
      - Negative
  - If Calf
    - Record Dam as Negative

Retain in Herd

Pregnant cows/heifers may be carrying PI fetuses. Must test newborn calves ASAP.
BVDV Control Tools

- Diagnostic Assays/Strategies
- Vaccines
- Biosecurity Measures
Vaccination is a Tool Not Silver Bullet
Many case/field studies suggest “vaccine failure” w/respect to reproductive disease caused by BVDV.

- Antigenic variation
- Vaccine protocol
- Poor vaccine handling

Experimental studies also show that BVDV vaccines are not 100% efficacious in preventing reproductive disease.
## Fetal Protection Against BVDV

<table>
<thead>
<tr>
<th>Study</th>
<th>Vaccine Virus</th>
<th>Challenge Virus</th>
<th>Vaccinates*</th>
<th>Controls*</th>
<th>Percent Protected</th>
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<tbody>
<tr>
<td>Mclurkin et al 1975</td>
<td>Killed 1</td>
<td>CP 1</td>
<td>12/14</td>
<td>0/5</td>
<td>86%</td>
</tr>
<tr>
<td>Harkness et al 1985</td>
<td>Killed</td>
<td>9 CP 1</td>
<td>7/11</td>
<td>0/11</td>
<td>64%</td>
</tr>
<tr>
<td>Meyling et al 1987</td>
<td>Killed 1</td>
<td>CP 1</td>
<td>2/8</td>
<td>0/5</td>
<td>25%</td>
</tr>
<tr>
<td>Cortese et al 1998</td>
<td>MLV 1</td>
<td>NCP 1</td>
<td>10/12</td>
<td>0/10</td>
<td>83%</td>
</tr>
<tr>
<td>Brock et al 2001</td>
<td>MLV 1</td>
<td>NCP 2</td>
<td>11/19</td>
<td>0/6</td>
<td>58%</td>
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<tr>
<td>Zimmer et al 2002</td>
<td>Killed CP and NCP</td>
<td>3 NCP 1</td>
<td>7/9</td>
<td>0/15</td>
<td>78%</td>
</tr>
<tr>
<td>Zimmer et al 2002</td>
<td>Killed CP and NCP</td>
<td>3 NCP 1</td>
<td>5/15</td>
<td>0/15</td>
<td>33%</td>
</tr>
<tr>
<td>Patel et al 2002</td>
<td>Killed CP1</td>
<td>NCP 1</td>
<td>9/11</td>
<td>0/7</td>
<td>81%</td>
</tr>
<tr>
<td>Dean et al 2003</td>
<td>MLV 1</td>
<td>NCP 1</td>
<td>25/27</td>
<td>0/13</td>
<td>92%</td>
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<tr>
<td>Fairbanks et al 2004</td>
<td>MLV 1/2</td>
<td>NCP 1</td>
<td>18/18</td>
<td>0/10</td>
<td>100%</td>
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<tr>
<td>Fairbanks et al 2004</td>
<td>MLV 1/2</td>
<td>NCP 2</td>
<td>18/19</td>
<td>0/8</td>
<td>95%</td>
</tr>
<tr>
<td>Grooms 2004</td>
<td>Killed 1/2</td>
<td>NCP 1/2</td>
<td>11/15</td>
<td>0/14</td>
<td>73%</td>
</tr>
</tbody>
</table>
Summary

- Important and Prevalent Virus in the dairy and beef industry
- Many clinical manifestations
  - Reproductive losses
  - Other manifestations
- Integrated Control Program
  - Vaccination
  - Biosecurity
  - Seek and destroy PI’s
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