# MANAGING BVDV RISK FACTORS FOR OPTIMUM DAIRY HERD HEALTH

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## The National Centers for Animal Health (NCAH)

Combines three agencies under one roof

- **National Animal Disease Center (NADC)**
- National Veterinary Services Laboratory (NVSL)
- Center for Veterinary Biologics (CVB)

# Managing risk

- Define the risk
- Determine extent of problem
- Estimate Cost/Benefit
  - Proactive
  - Reactive
- Identify workable options
  - One size does not fit all

# Disease Control

- **Nonspecific** means
  - Control stress
  - Nutrition
  - Housing
  - Biosecurity/Biocontian ment
- **Specific** targeted control
  - Surveillance for pathogens
  - Vaccination

Defining the risk

## Know your enemy

- Bovine viral diarrhea viruses
  - Two species
    - BVDV1 and BVDV2
  - Two biotypes
    - Cytopathic and noncytopathic
  - Wide host range
    - All even toed ungulates
  - Wide range of clinical presentations
    - Reproductive disease
    - Respiratory disease
    - Enteric disease
    - **Immunosuppresssion**

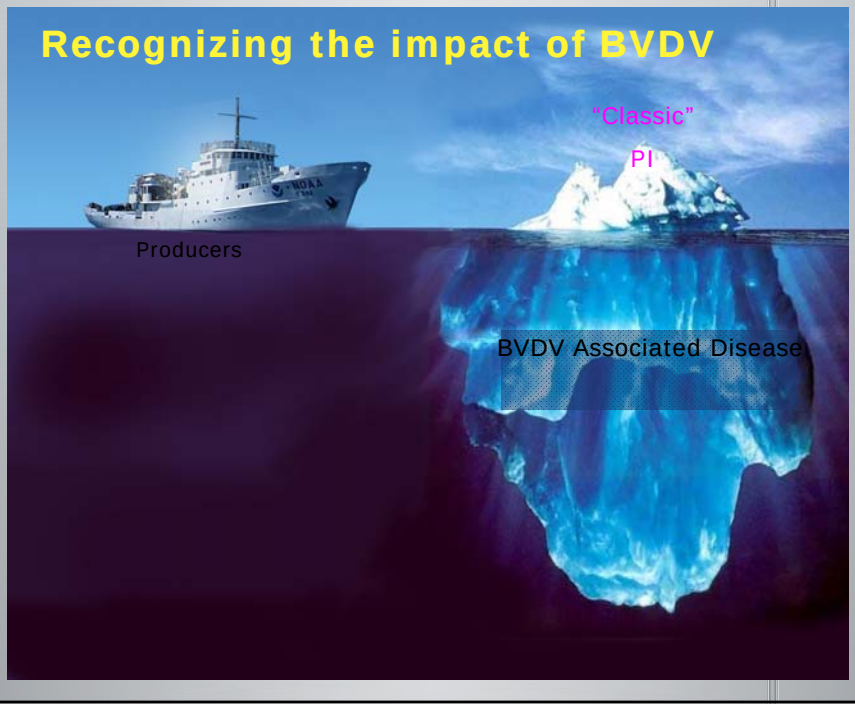
## Why bother with bovine viral diarrhea virus (BVDV)?

- What are the odds of it showing up in my operation?
- What happens if it does show up?

# Likelihood of coming in contact with a BVDV PI calf

| Number of Calves Introduced | PI Prevalence Level in Source Calves | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0.10% | 0.15% | 0.20% | 0.25% | 0.30% | 0.35% | 0.40% |
| 50 | 4.9% | 7.2% | 9.5% | 11.8% | 13.9% | 16.1% | 18.2% |
| 100 | 9.5% | 13.9% | 18.1% | 22.1% | 26.0% | 29.6% | 33.0% |
| 250 | 22.1% | 31.3% | 39.4% | 46.5% | 52.8% | 58.4% | 63.3% |
| 500 | 39.4% | 52.8% | 63.2% | 71.4% | 77.7% | 82.7% | 86.5% |
| 1,000 | 63.2% | 77.7% | 86.5% | 91.8% | 95.0% | 97.0% | 98.2% |
| 2,500 | 91.8% | 97.7% | 99.3% | 99.8% | 99.9% | 100.0% | 100.0% |
| 5,000 | 99.3% | 99.9% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |
| 10,000 | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |

slide courtesy of John Currin



# Estimating BVDV losses

- Effects on neonate
  - What doesn't kill you does not necessarily make you stronger
- Effects on feed conversion/milk production
  - Presence of PI
- Increased severity of concurrent or subsequent infections
  - Increases virulence of other pathogens
  - Hampers innate immune response. Slows acquired immune response
- "Silent" reproductive problems
- I don't have BVDV losses because I vaccinate

Understanding the problem

# What does BVDV do?

- ✓ Primarily infects immune system
- ✓ Acute disease
  - ✓ Severity dependent on:
    - ✓ Virulence of of theViral Strain
    - ✓ Immune Status
    - ✓ Reproductive Status
    - ✓ Presence of other pathogens
- ✓ Persistent infection
- ✓ Increases virulence of other pathogens
  - ✓ Depresses immune response
  - ✓ Directly interacts when cells are co-infected

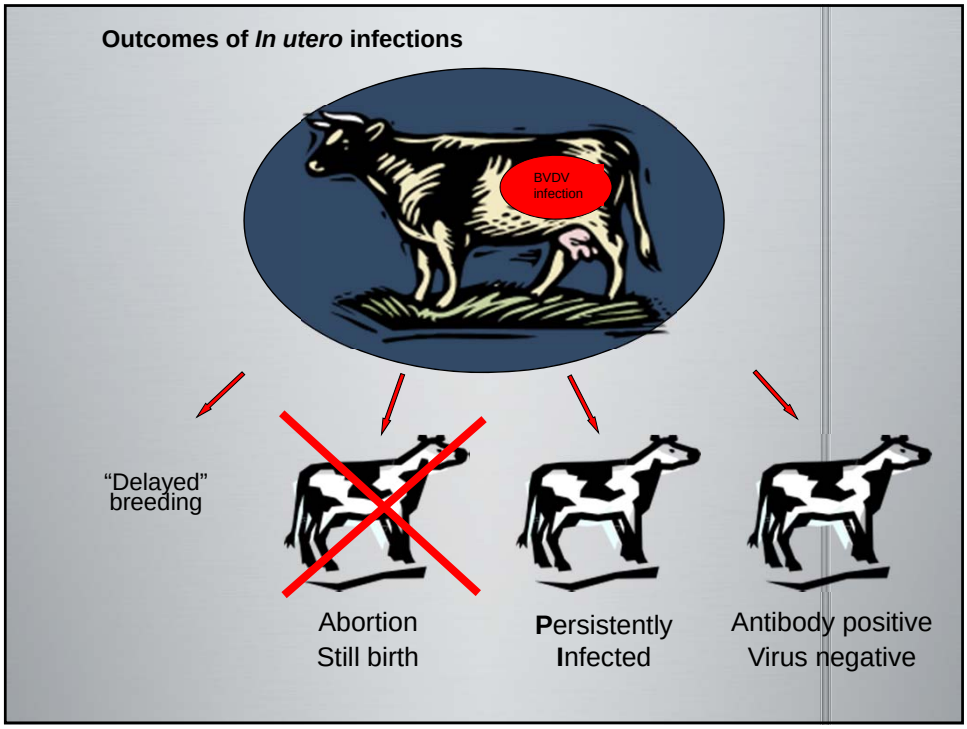
Understanding the problem

## How does BVDV do it?

- Direct or indirect contact with mucus membrane
  - Oral/Nasal
  - Mucus membranes of reproductive tract
- Limited replication in epithelial cells of mucus membrane leads to infection of draining lymph nodes
- Infects lymphoid cells (including progenitor cells)
- May progress to endocrine tissues, reproductive tissues and lung

## Persistent infections: The gift that keeps on giving

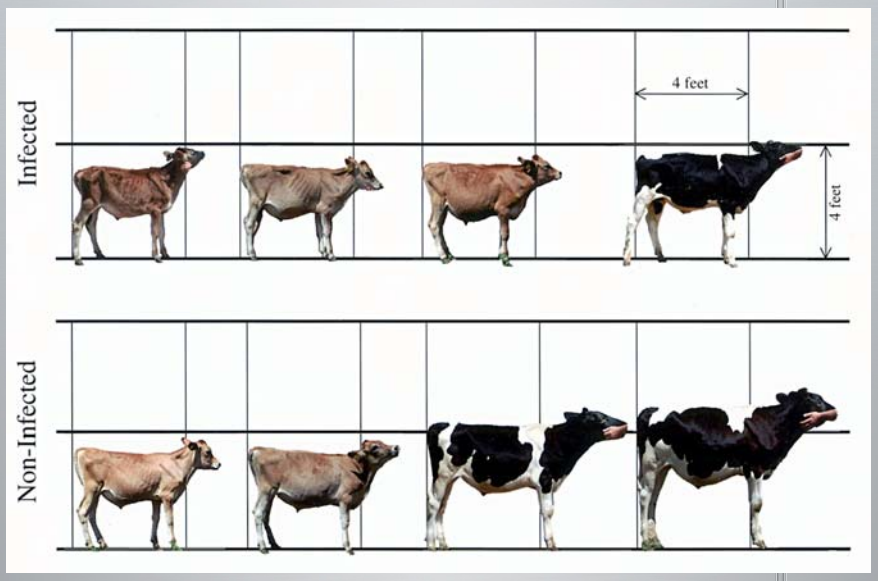
Result from in utero exposure to noncytopathic BVD



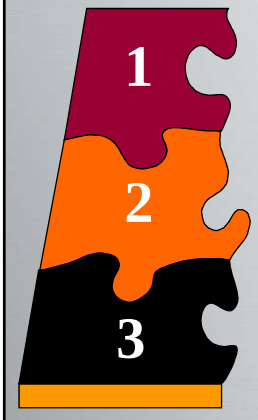

# Prolonged effects of infection

- Severe acute infections in neonates
- Revealed by comparison of growth rates following infection
  - All animals cleared virus by 14 days post inoculation

30 days post infection




## Simple targeted BVD control




Surveillance to detect

Biocontainment to affect, Biosecurity to protect

Vaccination to keep in check

Slide courtesy of D. Givens, Auburn Univ.

# Surveillance and Detection

## Detection of BVDV

- Cannot rely on history, clinical presentation or postmortem
- Accurate and definitive detectioin depends on laboratory diagnosis
- Standard for determination of PI status is 2 positive tests done on samples collected 3 weeks apart

# Detection target

- **Replicating virus**
  - Virus isolation
- **Viral proteins**
  - IHC
  - ACE
- **Viral genomic material**
  - In situ hybridization
  - Conventional PCR
  - Real time PCR
- **Antibodies against BVDV**
  - Serum neutralization
  - Antibody ELISA

# Virus isolation (VI)

- Historically considered gold standard
- Detects live virus
- Sample type
  - Wide range
    - Whole blood, buffy coat, serum, nasal swabs, macerated tissues
- Samples may be frozen

# Advantages of VI

- Target is biologically significant
- Further analysis can be done on isolated virus
- Isolation in not linked to a specific pathogen
  - You can find things for which you are not looking

# VI drawbacks

- Expensive
- Slow
  - Minimum 2 weeks
- Picks up acute and PI infections
- Passive antibodies may interfere with isolations from serum
- Must use reagents screened for BVDV antibodies or BVDV
- Requires relatively high level of expertise

# Immunohistochemistry (IHC)

- Based on binding of monoclonal (Mab) or polyclonal antibodies
- Fixed or frozen tissue sections or fixed cultured cells
- Tissue of choice - ear notch

# IHC Advantages

- Can see association of virus with lesions
- Not affected by passive antibodies
- Some pathologists think they can differentiate acute from PI

# IHC drawbacks

- Requires a relatively high level of expertise
  - Reliability increases with the experience and expertise of pathologist
- Mishandling of tissues will affect test
- Yes or no answer
  - Can't genotype

# Antigen capture ELISA (ACE)

- Commercial kits available
- Samples
  - Ear notches, serum, buffy coat, nasal swabs, lymphoid tissues

# ACE advantages

- Quick
- Requires least amount of expertise of all currently available tests
- Can pool samples
  - Not recommended by manufacturer
- Not affected by passive antibodies

# ACE drawbacks

- Can’t genotype
- Better at picking up PI’s but can also pick up acutes

# Polymerase chain reaction (PCR) based tests

- Coventional PCR
  - Sequence specific primers
  - Product visualized by agarose gel electrophoresis (identified by size)
  - Requires less technology
- Real time PCR
  - Sequence specific primers
  - Product identified by binding of sequence specific probe
  - More sensitive
  - Requires more fine tuning

# Advantages of PCR based tests

- Sensitive
- Fast
- Commercial kits are becoming available
- Samples may be pooled*
- Can quantitate target
- Can differentiate species

# PCR Drawbacks

- Can't differentiate replicating virus from inactivated virus or virus fragments
- Requires technical skill, good laboratory biosecurity and relatively expensive equipment

# To pool or not to pool

- May be cheaper (initially)
  - Penny wise and pound foolish
  - Initial cost vs timely identification and accuracy
- Surveillance or etiology
- Type of operation

# Life isn't perfect

Balancing sensitivity and specificity

## Test parameters

- Range
  - Conservation of target
- Sensitivity
  - Detects all positives
- Specificity
  - Ignores all negative (no false positives)

## Sensitivity and specificity analogy

- Baseball = sample
- Batter = test
- Plate = test parameters (definition of positive and negative)

## Batter performance

- Success
  - Swings at strikes*
    *In this analogy if you swing at a strike you get a hit
  - Doesn't swing at balls
- Failure
  - Doesn't swing at strikes
  - Swings at balls

# Unacceptable batter behavior

- Swings at all pitches
  - Doesn't miss a strike (high sensitivity)
  - Swings at all balls (low specificity)

# Unacceptable batter behavior

- Swings at no pitches
  - Doesn't hit any strikes (high specificity)
  - Doesn't swings at any balls (low sensitivity)

## No batter bats 1000

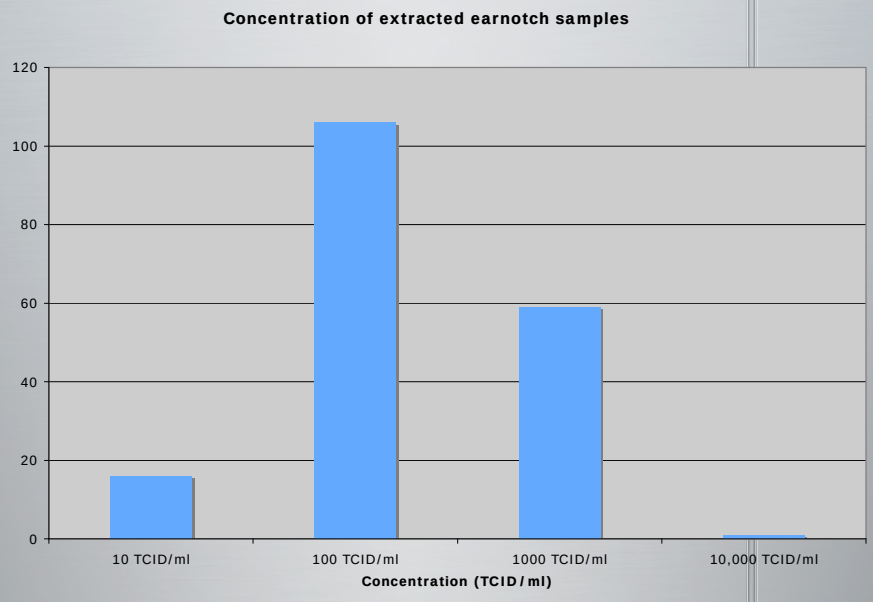
- There is a balancing act between sensitivity (no false negatives) and specificity (no false positives)

## Added level of difficulty with BVDV

- Detecting outbreaks of other pathogens
  - Just need to demonstrate virus is present for diagnosis
  - Don't need to identify every infected animal
- Detecting PI's
  - Desirable to identify every single PI animal

# A short history of pooling

- Ridpath et al. PCR primers for BVDV
  - 1994 - 140 isolates
  - 1998 - 345 isolates
- Kennedy et al. Pooled conventional PCR
  - 2005 - 4 ear notches (3 pools)
- 2006 numerous laboratories unable to generate reproducible results using pooled ear notch samples for PCR

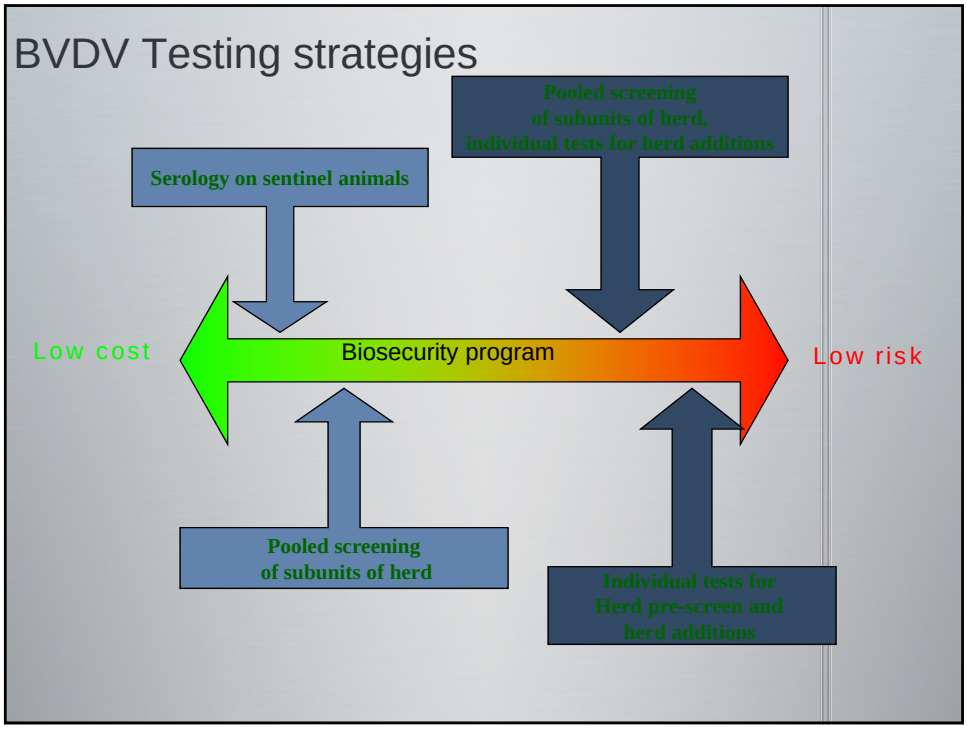


# What do you do with a PI?

- Must be removed
  - Do not send to sale barn
  - Market weight
    - Directly to slaughter
    - Poses no threat to humans
  - Below market weight
    - Euthanize
    - Put in biosecurity measures and feed to market weight
      - May be loosing proposition

# Detecting exposure - Serology

- Serum antibody based tests
  - Serum neutralization
  - Antibody ELISA
- Indicates exposure but not source of exposure
  - Can't differentiate MLV vaccination and natural exposure
- Need to be able to detect antibodies against both BVDV1 and BVDV2

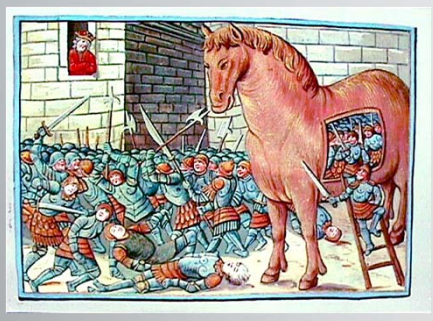



## Biocontainment/Biosecurity

# Source of infection

- Frequently PI animal
- Other possibilities
  - Pooled colostrum
  - Fetal bovine serum
    - Embryo transplant
    - Vaccines
- Semen
- Wildlife

# Recognizing possible PI's



## "I never thought it would be a problem"

- Purchasing bred heifers
- Using a heifer raiser
- Using colostrum from outside sources
- Purchasing bucket calves
- Sharing stock trailers
- Taking non vaccinated animals to cattle shows or 4-H fairs

# Vaccination

Raising herd resistance

## Peak Times of BVDV Infection

- ✓ Fetal Infections
  - ✓ <125 days may get PI
  - ✓ >125 days may have congenital defects
- ✓ 6 Months
  - ✓ End of passive immunity
- ✓ Mixing at stockyards and sale barns
  - ✓ Exposure to new strains, stress
- ✓ Entrance into breeding/milking herd
  - ✓ Exposure to new strains

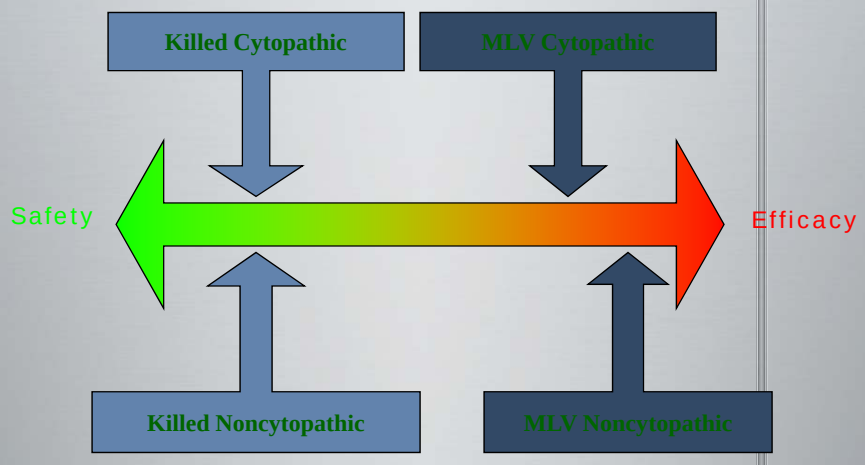
## Why do vaccines fail?

- Antigenic variation
  - Vaccine components should reflect viruses currently circulating in field
- Need time for immune response to develop
  - 10 to 14 days minimum
- Challenge occurs after duration of protection has expired
- Protection levels not high enough

# Vaccination strategy

- Provide protection prior to peak vulnerability
- Practical considerations
  - Cost
  - Safety
  - Management practices
- Stress will reduce vaccine response

# BVDV Vaccines




Slide courtesy of D. Givens, Auburn Univ.

## Vaccination to keep in check

**B. Question:** How can vaccination for BVDV be used most effectively to minimize the negative impact of disease on my farm?

***All vaccines should be used according to label directions. Please note that the least reliable vaccination protocols do not follow label directions. These inappropriate protocols provide no significant protection against disease.***

**Vaccination of calves to prevent subsequent disease:**

Least Reliable ↑ ↓ Most Reliable

| | |
|---|---|
| 1. | ∅ Vaccination prior to four months of age with a single dose of killed virus administered to healthy calves that nursed adequate colostrum. |
| 2. | ∅ Vaccination after four months of age with a single dose of killed virus immediately before weaning, transport, and commingling. |
| 3. | Vaccination prior to four months of age with a single dose of modified-live virus administered to healthy calves that nursed adequeate dolostrum. |
| 4. | Vaccination after four months of age with two doses of killed virus two to four weeks apart on the farm of origin immediately before weaning, transport, and commingling. |
| 5. | Vaccination after four months of age with a single dose of modified-live virus immediately before weaning, transport, and commingling. |
| 6. | Vaccination after four months of age with two doses of killed virus four weeks apart on the farm of origin at least two weeks before weaning, transport, and commingling. |
| 7. | Vaccination after four months of age with a single dose of modified-live virus at least two weeks before weaning, transport, and commingling. |
| 8. | Vaccination after four months of age with two doses of modified-live virus four weeks apart on the farm of origin immediately before weaning, transport, and commingling. |
| 9. | Vaccination after four months of age with two doses of modified-live virus four weeks apart on the farm of origin at least two weeks before weaning, transport, and commingling. |

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## Vaccination to keep in check

**Vaccination of heifers and cows to prevent reproductive losses:**

Least Reliable ↑ ↓ Most Reliable

| | |
|---|---|
| 1. | ∅ Vaccination of heifers and cows each year prior to breeding with a single dose of killed virus . |
| 2. | Vaccination of heifers with two doses of killed virus at least 30 days before initial breeding, without annual revaccination. |
| 3. | Vaccination of heifers with a single dose of modified-live virus at least 30 days before initial breeding, without annual revaccination. |
| 4. | Vaccination of heifers with two doses of modified-live virus at least 30 days before initial breeding, without annual revaccination. |
| 5. | Vaccination of heifers with two doses of killed virus at least 30 days before initial breeding, and annual revaccination of cows with a single dose of killed virus at branding or weaning . |
| 6. | Vaccination of heifers with two doses of killed virus at least 30 days before initial breeding, and annual revaccination of cows with a single dose of killed virus prior to breeding . |
| 7. | Vaccination of heifers with a single dose of modified-live virus at least 30 days before initial breeding, and annual revaccination of cows with a single dose of killed virus at branding or weaning . |
| 8. | Vaccination of heifers with a single dose of modified-live virus at least 30 days before initial breeding, and annual revaccination of cows with a single dose of modified-live virus at branding or weaning . |
| 9. | Vaccination of heifers with a single dose of modified-live virus at least 30 days before initial breeding, and annual revaccination of cows with a single dose of modified-live virus prior to breeding . |
| 10. | Vaccination of heifers with two doses of modified-live virus at least 30 days before initial breeding, and annual revaccination of cows with a single dose of killed virus at branding or weaning. |
| 11. | Vaccination of heifers with two doses of modified-live virus at least 30 days before initial breeding, and annual revaccination of cows with a single dose of modified-live virus at branding or weaning . |
| 12. | Vaccination of heifers with two doses of modified-live virus at least 30 days before initial breeding, and annual revaccination of cows with a single dose of modified-live virus prior to breeding . |

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## Vaccination to keep in check

**Vaccination of bulls to prevent amplification and spread of virus:**

Least Reliable ↑ ↓ Most Reliable

| | |
|---|---|
| 1. | ∅ Vaccination of bulls each year prior to breeding with a single dose of killed virus. |
| 2. | Vaccination of bulls with two doses of killed virus at least 30 days before initial breeding, without annual revaccination. |
| 3. | Vaccination of bulls with a single dose of cytopathic, modified-live virus at least 30 days before initial breeding, without annual revaccination. |
| 4. | Vaccination of bulls with two doses of cytopathic, modified-live virus at least 30 days before initial breeding, without annual revaccination. |
| 5. | Vaccination of bulls with two doses of killed virus at least 30 days before initial breeding, and annual revaccination with a single dose of killed virus prior to breeding. |
| 6. | Vaccination of bulls with a single dose of cytopathic, modified-live virus at least 30 days before initial breeding, and annual revaccination with a single dose of modified-live virus prior to breeding. |
| 7. | Vaccination of bulls with two doses of cytopathic, modified-live virus at least 30 days before initial breeding, and annual revaccination with a single dose of modified-live virus prior to breeding. |

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