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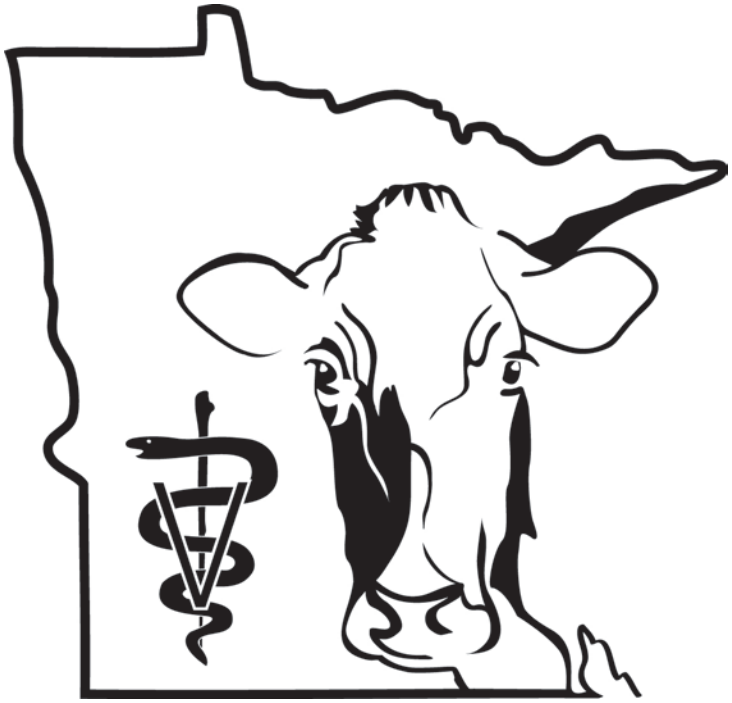

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BVD: A Review of Epidemiology, Vaccines, and Diagnostic Tests

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Bovine Viral Diarrhea (BVD) virus was first described in New York State in 1946. Over sixty years later, bovine practitioners and livestock producers are continuing to manage BVD through vaccination, diagnostic tests, and biosecurity protocols. The goal of this proceeding is to review the recent epidemiology of BVD persistent infection (BVD PI), current BVD vaccines, and the variety of diagnostic tests and testing strategies.

The prevalence of BVD PI continues to remain low. A few epidemiological studies estimating the prevalence of BVD in the United States indicate that regional prevalence of infected herds (those containing at least 1 BVD PI) has never exceeded 20%. Houe determined that in Michigan dairy herds the prevalence of at least one PI animal was 15% (3/20 herds) [1]. The overall prevalence of BVD positive bulk tank milk was 12.4% in over ninety Northeast dairy herds[2]. It is important to remember that bulk tank PCR does not detect non-lactating PI cows and heifers within the herd and testing milk can result in an underestimation of true PI prevalence and endemic infections.

Persistently infected cattle are rare and often represent less than 1% of the cattle within a herd. The prevalence of BVD PI across all Michigan Dairy Herds was 0.11%. The prevalence of BVD PI in central plains beef feedlots ranged from 0.3-0.4%.[3,4] Less than 1% of tissues submitted to the MVDL are BVD positive and approximately 0.3% of Holstein bull calves purchased and fed by Minnesota dairy beef producers are BVD PI (MVDL 2006& 2007 data).

Although PI cattle are rare, they appear to be surviving longer and are increasingly more difficult to detect visually. Historically, most PI cattle never reached maturity and often died early in life. As more feedlots are screening for BVD PI, they are finding that more than half of weaned PI beef cattle mature to market weight.

BVD Epidemiology Summary:

1.) Herd prevalence of BVD PI is low and is estimated to be below 20%.
2.) Approximately 0.2-0.4% of cattle are BVD PI.
3.) PI cattle appear to be surviving longer than expected.

BVD PI cattle and virus characteristics:

PI cattle are the primary reservoir for BVD virus. PI's excrete virus in numerous excretions and secretions including feces, urine, milk, nasal discharge and blood. PI cattle shed significantly more virus than acutely and transiently infected animals. Although the PI excrete and secrete large amounts of virus, PI transmission within dairy herds can be slow under dry-lot conditions [5]. Natural exposure of virus from PI cattle to naïve cattle can be accelerated by multiple uses of needles, palpation sleeves, implanting guns, nose tongs,

McGrath pumps, and other tools. Palpating a PI heifer followed by palpating short-bred heifers (40-120 DDC) is a good way to infect naïve cattle and their fetuses resulting in more PI calves. Likewise, if a PI resides in a group of transition cows, the use of needles, palpation sleeves, pumps, Frick speculums, and other physical objects is a good method of transmitting the virus to naïve cattle. Virus transmission at cattle water troughs has consistently been determined to be a method of transmission. Even if the cattle have been vaccinated, the overwhelming amount of virus in secretions and excretions can exceed the host's ability to prevent infection and subsequent viremia leading to fetal infections.

BVD virus derives its capsule from the host cell membrane as the virus exits the cell. Because of this, the virus is very susceptible to many detergents and disinfectants. Although BVD virus is susceptible to common disinfectants, the virus can tolerate moderate variations in pH. The virus usually only survives outside the host for a few days in the bovine environment.

BVD PI cattle and virus characteristics:

1.) PI's are the source of BVD and virus transmission stops in the absence of PI.
2.) Virus transmission from a PI animal to naïve animals can be accelerated by common instruments.
3.) The virus can be inactivated by many disinfecting solutions and does not persist in the environment for extended periods.

Economic impact of BVD:

The economic impact of BVD is variable due to wide variations in virus virulence. A Canadian study examined the direct production losses and treatment cost for BVD in dairy herds and calculated the cost at $48 per animal/year [6]. Losses due to severe, acute, type 2 BVD on Ontario dairy farms from 1993-1995 had an estimate economic loss ranging from $40,000 to $100,000 per herd (average herd size 50-100 cows). Losses in those acute BVD infections include dead cattle, decreased milk production and abortions[7]. A large beef feedlot trial in Western Kansas concluded that the losses per animal exposed to a BVD PI was approximately $65 per animal exposed and the losses per head across the entire feedlot (0.4% PI prevalence) was approximately $40. In beef feedlots, the largest losses were due to decreased feed efficiency, decreased average daily gain, and increase in cost of gain. Health parameters and increased treatment costs had less of a negative economic impact than feed efficiency and growth.

BVD Economic Summary:

1.) Economic cost of a BVD infection ranges from $40-$200 per exposed animal.
2.) Wide variations in virus virulence results in wide variations of estimated losses.
3.) In feedlot cattle, reduced feed efficiency and daily gain were most significantly affected.

BVD Persistence:

Although the herd prevalence of BVD and BVD PI remains low, the virus can persist in non-vaccinated and vaccinated cattle herds. There appears to be three factors contributing to BVD

persistence and they are; 1) herd consolidation resulting in larger herds, 2) incomplete vaccine efficacy and, 3) a virus that is different from those in vaccines.

Consolidation of the dairy industry has resulted in fewer and larger herds. Many of these herds are assembled from numerous smaller farms, heifer growers, order buyers and sale barn facilities. As the number of susceptible candidates in a population increases, the odds that BVD will infect and produce a PI calf also increases. Simply stated, if you increase the number of susceptible fetuses, you increase the odds of producing another PI calf.

It is important to remember that BVD persists in cattle populations by finding a short bred fetus (40-120 DCC), infecting it, and therefore resulting in another PI calf. The source of fetal infection is almost always by direct exposure to another PI animal; however, diagnosis of a PI animal today indicates fetal exposure many months prior to the day the calf was born. Diagnosis of a PI indicates *historical* exposure.

Vaccination of the dam provides partial and not complete protection of the fetus [8]. Many commercially available vaccines contain BVD stains type 1a and 2a, but no vaccines currently contain BVD strain type 1b. Furthermore, there is not significant variation between many of the vaccines strains as many contain the same strains. The following is a table of a few MLV BVD vaccines used today.

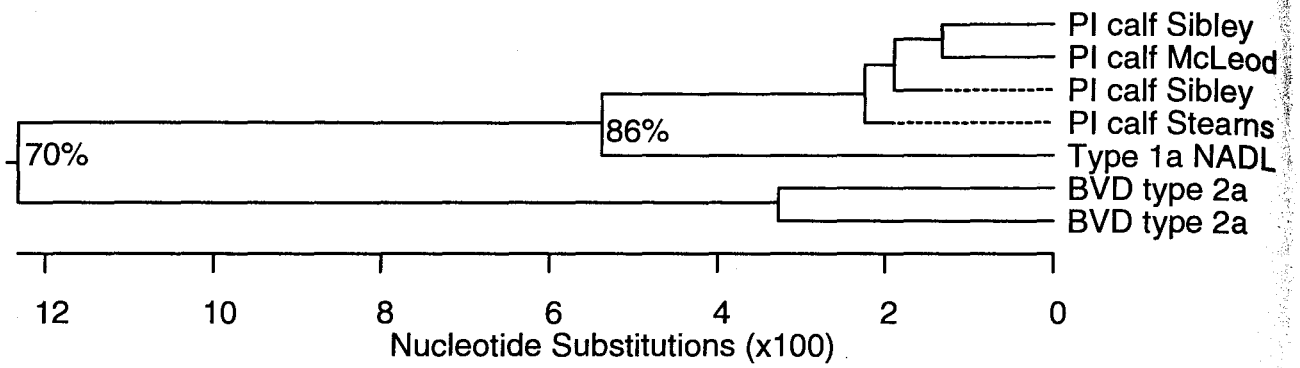
Modified Live Vaccines:

Tradename	Genotype/Biotype	Strain	Manufacturer
Bovashield Gold	1a cp	NADL	Pfizer
	2a	24515-1373	
Express 5	1a cp	Singer	Boehinger Ingelheim
	2a cp	296	
Pyramid	1a cp	Singer	Fort Dodge
Titanium	1a cp	C24V	AgriLabs
	2a cp	296	

BVD is a single stranded RNA virus. Like other RNA viruses (Influenza, PRRSV,etc), the virus does not have a "proof-reading" component and constantly "drifts and shifts."

Eighty percent of the BVD viruses isolated from PI cattle are BVD type 1b [9]. BVD type 1b is approximately 85% similar to BVD type 1a, and although this may appear quite similar to type 1a, this difference between strains is detected in a small, highly conserved region of the virus (5' UTR). The differences between type 1a and 1b is potential more diverse in regions of the virus that are important for stimulating immunity (E2 region glycoprotein region). Below is a dendrogram of BVD isolated from BVD PI dairy calves in Minnesota. All four calves are from large dairies that vaccinated with commercially available vaccines according to label directions. All four calves are infected with a strain of BVD different from 1a or 2a. This strain may be type 1b, but definitive classification has not yet been determined. For comparison, the BVD type 2a stain is 70% similar to BVD type 1a. All four PI calves are

"healthy" and at least one-year-old. If the PI calves would have remained on the dairies they were born, they would currently be in the heifer breeding pen.



Dendrogram: A comparison of BVD strains. The type 2a and 1a (NADL) strains are viruses used in BVD SN testing. The four PI calves are from four different dairy farms in Minnesota.

Diagnosing BVD:
In my opinion, the largest challenge facing veterinarians and producers in regards to BVD is...*How can I accurately determine if a given herd contains a PI animal?* If the herd prevalence of BVD is low (<20%), what cost-effective, accurate strategies are available to determine if the herd is endemically infected and contains a PI animal?

Serology (Detecting BVD antibody):
A few European countries have eradicated BVD. Because many European countries do not vaccinate for BVD, they were able to detect infected herds by screening bulk tank milk for BVD virus antibody. If a European herd had BVD antibody in bulk milk, there was a high probability that a PI was in the herd. All cattle in herds that had BVD positive antibody milk were screened for BVD PI with individual antigen test including IHC and AgELISA. Almost all bulk milk in the United States is positive for BVD antibody due to the widespread use of vaccines or exposure to virus.

Acute and convalescent serology is a popular and reliable way to detect virus exposure in many animal species. BVD vaccination has almost completely confounded interpretation of BVD SN titers. Most of the BVD that has been detected in PI cattle today is BVD type 1b and we don't know how well the current type 1a and type 2a viruses react with 1b serum antibody in the SN tests. An additional drawback of serology is that virus transmission in dairy herds is slow and determined when an animal is infected can be problematic as many BVD infections are subclinical.

Serological evaluation of non-vaccinated sentinels calves has been attempted in both dairy and beef herds and has been marginally successful[10, 11]. The prevalence of seropositive calves serves as indirect evidence of virus exposure and the likelihood of a PI calf within the

herd. In Michigan dairy herds, non-vaccinated 6-12-month-old heifers had a sensitivity of 66% and a specificity of 100% for detecting herds that have PI cattle. The limited sensitivity of sentinel calves may be a result of low stocking density, limited exposure to a BVD PI calf due to the variety and size of management groups in the herd, and the commingling or fence-line contact of cattle with adjacent herds. Passively acquired maternal antibodies also can confound interpretation when calves are sampled prior to complete antibody decay.

Serology can still be an effective and efficient way to detect circulating virus-and the presence of BVD PI within a herd. The "hitch" of serology in vaccinated herds is that detecting BVD antibody has the most value in "wet" newborn calves prior to colostrum feeding (precolostral serum sampling). Calves born with BVD serum antibodies prior to colostrum feeding gives clear indication that the dam was exposed to a BVD during the last 5 months of gestation and the fetus had seroconverted to BVD *in utero* (often referred to BVD congenital infection – BVD CI). The primary advantage of precolostral serum sampling is that there are 8-10 times more calves that seroconvert to BVD CI then those born PI; therefore, fewer calves need to be sampled to detect circulating virus and the presence of BVD PI. Also, there is no acute and convalescent sampling needed. In herds with endemic BVD virus infection, approximately 8-10% of calves born are positive to BVD antibody prior to colostrum feeding. If newborn calves are seropositive to BVD, the veterinarian and owner can investigate where the dam was during the last 5 months of gestation (DDC). Any animal that had contact with the dam carrying the CI calf during the last 5 months of gestation may have been BVD PI.

Determining BVD PI cattle with bulk tank PCR is a popular strategy due to the ease of sample collection[12]. When sampled correctly, PCR on bulk milk can detect one PI in a group of 300. Limitations of bulk milk PCR include the inconsistent sample collection from in-line sampling devices and the test fails to detect non-lactating cattle and PI cattle in the youngstock population.

Detecting BVD virus (IHC, AgELISA, RT-PCR, virus isolation):
Due to the widespread use of vaccination and the effect it has had on interpreting serology, the industry has adopted an "all-antigen" testing strategy.

Numerous diagnostic tests have been developed to accurately detect BVD PI. Numerous studies have compared PCR, AgELISA, and IHC and many have demonstrated that all three consistently detect PI cattle. Because ear notches are a convenient sample to collect, IHC and AgELISA on ear notches are popular. AgELISA appears to be extremely robust across many labs due to a commercially available test kit manufactured by IDEXX. Fresh frozen ear notches can be stored for up to a week or more before testing and AgELISA has the added convenience of not having to work with and store formalin.

RT-PCR has received substantial negative press over the last year. Many labs have indicated many false negative results (reporting PI's as negative) in individual and pooled samples, while other labs continue to offer the test and indicate high sensitivity. BVD PCR protocols vary significantly between laboratories. Because of this, many labs have abandoned PCR

while others continue to offer a variety of PCR tests. If you want to run PCR tests on serum or ear notches, contact the laboratory and ask for sensitivity data.

BVD diagnostics summary:

Herd status

1.) Non-vaccinated sentinel calves can be used detect BVD PI cattle in the youngstock population
2.) Bulk milk PCR will detect lactating PI cattle when milk is sampled correctly
3.) Precolostral sampling of newborn calves will detect circulating virus in late gestation cows and heifers

PI status

1.) Ear notches are popular samples due to ease of sample collection
2.) AgELISA on fresh ear notches is a robust test due to a universal testing procedure (IDEXX kit)
3.) The sensitivity of PCR varies between laboratories and consultation with the laboratory prior to testing is advised

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