COST ANALYSIS OF BVDV PI TESTING AND ERADICATION IN COW CALF HERDS

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Introduction

Bovine viral diarrhea virus (BVDV) infection is responsible for a variety of economically important syndromes in beef herds. Quantifying the economic benefit of removing BVDV persistently infected animals from a herd, and hence the value of diagnostic testing to achieve that goal, is an important consideration for veterinarians.

BVDV infection can cause a complex of disease problems, including respiratory disease, infertility and fetal infection.[2] Fetal infection can lead to early embryonic death, abortion, congenital defects, stunting, or the birth of persistently infected (PI) calves.[2] Persistently infected cattle are the result of *in utero* exposure to the noncytopathic biotype of BVDV prior to the development of a competent fetal immune system by about 125 days of gestation.[12,26,29,] Transplacental infection occurs with high efficiency during pregnancy, and if PI fetuses survive to term, they are continually viremic, but immunotolerant to homologous BVD virus.[16,41]

The prevalence of PI animals in the general cattle population has been estimated to range between 0.13% and 2.0%.[8,22,24,45] Differences in reported prevalence may be due to the population tested, the country/continent where the population was located and/or the diagnostic tests utilized. Persistent infection has a clustered distribution, which means a few herds may contain several PI cattle but most herds contain only non-PI cattle.[7,25] Clustering of multiple PI animals in a herd is due to exposure of numerous susceptible dams to a PI or transiently infected (TI) source of noncytopathic BVDV prior to day 125 of gestation.

The primary reservoir for and source of BVDV are cattle PI with BVDV, with TI cattle considered a less important source. Persistently infected animals are a much more efficient transmitter of BVDV than TI animals because they secrete much higher concentrations of virus for a much longer period of time. After a short latent period, TI animals experience a short period of viremia and virus is shed in body secretions and excretions from days 4 to 15 post-infection.[11,16] In contrast, PI animals usually have a very high and persistent viremia, and BVDV is shed continually from virtually all secretions and excretions including nasal discharge, saliva, semen, urine, tears, milk, and to a lesser extent, feces.[5,9,10,39] Horizontal transmission of the virus from either persistently or transiently BVDV-infected animals to susceptible cattle in direct contact may be via inhalation or ingestion of virus-containing body fluids.[16] In addition, air transmission from PI animals over short distances seems likely; however, when cattle are housed at greater distances from PI animals, the spread of infection is slow or absent.[44] Horizontal transmission of BVDV to seronegative cattle has been shown to occur after only one hour direct contact with a single PI animal.[43] Over-the-fence contact with a PI from neighboring cattle can also introduce BVDV into a susceptible herd.[32,41]

Suckling calves are commonly in contact with the breeding herd during early gestation, prior to the time the bovine fetus develops a competent immune system. As a result, PI suckling calves are considered to be the primary source of BVDV infection in breeding herds causing pregnancy loss, pre-weaning mortality and the induction of PI calves in the next generation.[16,29]

Although PI suckling calves are considered to be the primary reservoir for BVDV in a herd, PI adults can also be present in a herd. Adult PI animals are not as common because mortality of PI calves prior to and after weaning has been reported to be very high due to fatal congenital defects and secondary infections that cause enteritis, pneumonia, and arthritis.[29,30] However, 17% to 50% of PI calves may reach breeding age in some situations.[3,6,23] PI breeding females not only are a source of horizontal transfer of BVDV, but will always produce a PI calf themselves.[22,29] Witttum *et al*., showed that 7% of PI calves were born to dams that were PI.[45] Meaning that while PI dams can be a direct cause of a small percentage of PI calves, a vast majority (93%) of PI calves are born to non-PI dams due to transient infection of the dam during gestation.[45]

Male PI calves will occasionally be selected for use as breeding bulls. The amount of BVDV excreted in the semen of persistently infected bulls is very high (10^4-10^6 $TCID_{50}$/ml).[40] BVDV-contaminated semen is an efficient horizontal transmitter of disease from bull to seronegative females.[38] If PI bulls are used for natural service, PI calves are not common, but seronegative cows may not be able to conceive. Once immunity has developed, cows can conceive and give birth to normal (non-PI) calves.[3,29] If PI bulls are used for AI, all or most seronegative females bred with the semen will become infected although most will not produce a PI calf.[34]

Circulating virus may exist in herds following removal of PI calves although the efficiency of virus transmission via transient infections alone is not high.[21] Limited data in dairies suggest BVDV may circulate in an unvaccinated herd for 2-3 years following removal of all PI animals.[3,21,33] The length of time for BVDV circulation in vaccinated beef herds without PI animals has not been reported.

Diagnostic Laboratory Tests to Identify PI Cattle

Cattle PI with BVDV can be identified by virus isolation from whole blood (buffy coat) or other tissue, immunohistochemistry (IHC) staining of viral antigen in skin biopsies, antigen-capture enzyme-linked immunosorbent assay (ELISA), and polymerase chain reaction (PCR) methods.[15] Persistently infected animals produce an exceptionally large number of BVDV particles that can be isolated from virtually any tissue sample. Virus isolation is considered to be very specific for BVDV infection; however, colostral antibodies may temporarily reduce the amount of free virus in the serum of young calves, making the test less sensitive in young calves.[10,37] In the presence of passively acquired BVDV antibodies, virus from PI calves cannot be detected in serum or whole blood by virus isolation. However, once maternal antibodies have disappeared, BVDV can be demonstrated repeatedly. Maternal antibodies had disappeared and BVDV could be isolated by six weeks of age in all four PI calves in one study,[10] and by eight weeks of age in all eleven PI calves in another study.[37] A few PI calves will develop neutralizing antibody and can clear the virus from serum. Therefore, virus isolation will only be possible from WBC samples, not serum in some PI cattle.[10] Virus isolation methods are labor intensive and take several days to complete. An additional shortcoming is that virus isolation may not differentiate between TI animals and PI animals, unless positive cattle are re-tested and remain positive at a later date (i.e. three weeks later).

An immunohistochemical (IHC) test for BVDV infection using skin biopsy samples, such as ear notches, is available that differentiates between PI animals and transient BVDV infections.[35] Transiently infected animals may have internal organ tissue samples that are IHC positive.

However, when skin samples were evaluated, transiently infected animals either had no staining, or staining was confined to the epidermal keratinocytes and follicular ostia, in contrast to PI cattle with antigen-positive staining cells in all layers of the epidermis, all levels of hair follicles, and the hair bulb.[35] This test is suitable for herd screening because samples can be taken from cattle of any age, sample collection is simple, the samples are stable for transport and handling, and the test is both sensitive and specific for BVDV PI cattle.[4,17,35] In addition, use of modified live vaccine does not appear to cause false positive IHC results when testing for PI animals.[14]

PCR testing for BVDV infection is more rapid than virus isolation and can detect virus in antigen-antibody complexes. PCR tests are sensitive and have been shown to differentiate between BVDV genotypes. However, a single BVDV positive blood (buffy coat) sample tested by PCR does not allow the diagnostician to differentiate between viremia from a postnatal acquired infection (and possibly MLV vaccination) and viremia due to being persistently infected. Because PCR tests can identify minute amounts of virus, this test can be used in pooled samples of serum or milk in surveillance programs.

Economic Cost of the Presence of PI Cattle in a Herd

The presence of PI animals in a breeding herd can result in decreased pregnancy percentage compared to herds with no PI calves.[45] This decreased pregnancy percentage could be due to ovarian dysfunction,[19,25] failure of fertilization,[18] early embryonic death,[1,23,31] and/or mid-gestation fetal loss[42] in cattle acutely infected with BVDV. Grooms *et al* found that BVDV could be isolated on days six and eight following infection with noncytopathic BVDV in ovarian stromal and macrophage-like cells, and oophoritis was evident from 6 to 60 days post infection.[19] McGowan *et al* reported that conception percentage, determined 20 days after insemination, was lower in heifers intranasally-infected with BVDV nine days before insemination compared to controls (44% vs 70%; P=0.055).[19] In addition, conception percentage was numerically lower in heifers exposed to a PI cow-calf pair four days after insemination than in unexposed controls (60% vs 79%; P=0.255).[31] The intranasally-exposed heifers also experienced significant embryo-fetal loss, resulting in a pregnancy percentage, determined 77 days after insemination, significantly lower than controls (33% vs. 79%; P=0.018).[31] Rufenacht *et al* found that dairy cows infected with BVD during the first 45 days of gestation (as indicated by seroconvertion to BVD during that time frame) had the same conception percentage as cows that either had previous exposure to BVD (seropositive for BVD by start of the trial) or that were not exposed to BVD during gestation (no seroconversion during trial). Similarly, BVD-exposure status did not influence late gestation pregnancy loss (>210 days). However, cows infected with BVD during mid-gestation (days 46-210) had greater pregnancy loss compared to those that were seropositive prior to breeding or that were not exposed to BVD during mid-gestation (pregnancy loss of 15.8% vs 6.1%; OR=3.1; P<0.02).[42]

In addition to decreased pregnancy percentage, reproductive efficiency can be decreased due to fatal congenital defects following fetal infection of BVDV between 100 and 150 days of gestation.[16] The teratogenic lesions associated with fetal infection with BVDV include microencephaly, cerebellar hypoplasia, hydranencephaly, hydrocephalus, defective myelination of the spinal cord, cataracts, retinal degeneration, optic neuritis, microphthalmia, thymic aplasia, hypotrichosis, alopecia, brachygnathism, growth retardation and pulmonary hypoplasia.[2]

Studies have reported a pre-weaning mortality proportion for PI calves of 20% to 83%, which can result in substantial loss in herds with a high prevalence of PI calves (i.e. 10%). However, overall mortality percentages between herds with or without PI calves were not statistically significantly different because of the low prevalence of PI calves within most PI-positive herds.[45] In herds with PI animals present, Larson *et al*., modeled scenarios both with and without a 10% negative effect on pre-weaning mortality percentage; and found that the greatest economic loss due to the presence of PI animals was decreased calving proportion with a lesser loss due to pre-weaning mortality.[28]

The result of an introduction of a PI animal into a beef herd (confined breeding and calving seasons) depends on the timing of the introduction relative to the breeding season and the resulting immunologic status of the herd during early gestation. Even in the absence of vaccination, the number of PI animals and the amount of BVDV infection in a herd seems to be self-limiting.[20] A likely scenario for a BVDV-exposed herd is to experience an initial peak of disease and then in subsequent months and years, to experience low-level chronic reproductive losses. If a PI animal enters the herd either by birth or by purchase near the start of the breeding season, a high percentage of the herd may not be immunologically protected to the degree necessary to prevent viremia, conception failure, abortion, or fetal infection. Once the PI animal is in contact with the breeding herd for a long enough period of time, the majority of the herd should become infected and seroconvert. Seropositive animals are less likely to have conception failures, abortions, or infected fetuses compared to seronegative animals. If no intervention is applied to the herd, the number of susceptible females the following year should be greatly decreased and the number of abortions and infected fetuses (both persistently infected and immunocompetent) should decrease. A model developed by Cherry *et al*. indicates that in continuous calving dairy situations, the proportion of PI animals in the herd will reach an equilibrium of about 0.9 to 1.2% in herds with no BVDV control procedures.[13]

Testing Strategies to Identify PI Cattle

Because the persistently infected animal is an important reservoir and transmitter of BVDV, control programs must first identify and remove these animals from the breeding herd. Because of vertical transmission of the virus from viremic dams to their fetuses, PI animals should be removed prior to the start of the breeding season in beef herds with a controlled breeding season. In order to find and remove PI cattle prior to the start of the breeding season, all calves, all replacement heifers, all bulls, and all non-pregnant dams without calves due to not becoming pregnant, aborting, or calf mortality must be tested for PI status.[27] Any female that is still pregnant at the time the herd is tested should be isolated from the breeding herd and kept isolated until her calf is tested and found to be negative.

If a herd has had confirmed PI calves, or if the history strongly suggests the presence of PI calves, the *a priori* assessment of PI prevalence is fairly high, making the predictive value of a positive test high enough one can conclude that the individual is a PI and the herd has PI animals present and a second confirmatory test may not be justified. In contrast, if the diagnostician has no *a priori* evidence of PI prevalence greater than a range of 0.3% to 0.5%, the predictive value of a positive test is low and a different confirmatory test may be advisable before making conclusions about the individual and herd. Once a calf is identified as PI, it should be euthanized or removed for slaughter and the dam should be tested. Most dams of PI calves are not PI

themselves, and if confirmed as non-PI, can re-enter the breeding herd because naturally acquired immunity is considered to prevent future fetal infections.[36] Dams identified as a PI, should be sold to slaughter immediately.

In most whole-herd testing situations, IHC testing of skin samples is the test of choice because it can be accurately performed on animals of any age and a single sample is all that is usually needed. Using virus isolation or PCR to identify PI cattle requires a second test three weeks following any positive samples to differentiate between transient viremia and PI with BVDV.

Economic Value of Diagnostic Testing To Identify and Remove PI Cattle

Determining the value of diagnostic testing depends on identifying the potential performance impact that a diagnosis and corresponding management intervention would have on a herd compared to an expected economic baseline without testing, given expected prevalence in the herd. The economic assessment is then made by quantifying the performance differences as manifested in enterprise analysis and expected changes in farm profitability.

Larson *et al*., used a 10-year (1991 to 2000) dynamic farm profitability simulation model that generates annual cash flow, balance sheet and income statements to compare three production scenarios: 1) herds with no PI calves, 2) herds with at least one PI calf present with a negative effect on pregnancy percentage, but no effect on pre-weaning mortality or weaning weight, and 3) herds with at least one PI calf present with negative effects on pregnancy percentage, pre-weaning mortality and weaning weight. Each scenario incorporated herd performance and economic interactions. Data from Wittum *et al*, which estimates the pregnancy percentages and pre-weaning mortality for herds with or without at least one PI calf present was used to model all three scenarios.[45] Because the Wittum study involved herds from five geographically diverse states and a fairly large number of herds positive for the presence of at least one PI calf (n=13), the authors assumed that the positive herds represented a cross-section of levels of herd immunity, gestational status and virus virulence combinations present in the U.S. Farm economic activity for each scenario was reported as return to fixed costs as determined by subtracting variable costs from income for each year of the evaluation. Herd size was not varied between the scenarios therefore more heifers needed to be retained in herds with at least one PI calf identified because of decreased pregnancy percentage.

Using cattle and feed prices for the 10 year period from 1991 to 2000, Larson *et al*., estimated that the average cost of having at least one PI animal present in a beef cow herd ranged from about $15 per cow exposed for breeding if the presence of a PI animal reduced pregnancy percentage from 92.7% to 89.6% (Table 1). And, if the presence of a PI animal increased pre-weaning mortality from 7.2% to 7.9% as well as reducing pregnancy percentage, the average cost of having a PI animal was estimated to be $20 dollars per cow exposed (Table 1).[28]

The model used by Larson *et al*. considers the cost of BVD infection to the cowherd to the point of selling the calves at weaning. Insufficient information is available to model the effects of the presence of PI BVD calves on pen or group performance post weaning. One could conjecture that PI BVD calves in a group of stocker or feedlot cattle could increase the morbidity, mortality and potentially decrease the growth and carcass performance of not only the PI calves, but also in-contact pen-mates. Because of the nature of the model used, the entire cost of BVD PI cattle

to the beef industry is not addressed, and therefore the values reported as costs to cowherds probably underestimates the cost of BVD PI cattle to the beef industry as a whole.

Table 1. Average cost over 10 years for the presence of BVDV PI cattle in a herd (Adapted from Larson *et al*, 2002)[28]

	10 Year Average	
	Return to Fixed Cost	Difference from Herd with No PI Cattle
No PI cattle present	$78.82	
At least 1 PI – reproductive effect only	$63.49	$15.33
At least 1 PI – reproductive and calf mortality effects	$58.66	$20.16

By doing a whole herd screening the initial year in herds where PI animals are known to be present, and screening all replacement animals (15% annual replacement rate) in subsequent years, the dollars available per test to equal the return to fixed cost of doing nothing is $61.32 to $80.64. This level of return indicates that whole herd screening and removal of PI cattle is economically justified if PI presence is known.

In herds where PI presence is not know, the economic benefit of testing to find PI animals must be evaluated in relation to the prevalence of herds with PI cattle present and the cost of whole-herd screening. Practitioners are able to categorize U.S. beef herds as high-risk for the presence of BVDV PI animals compared to randomly selected herds.[45] Wittum *et al* identified 48 veterinary practices from five geographically diverse states (Alabama, Nebraska, Nevada, North Dakota, and Ohio) that routinely provide veterinary services to commercial beef herds to participate in a BVD PI prevalence study.[45] Using a random-numbers table, 76 herds were randomly selected from client lists for evaluation of BVDV PI prevalence. In addition, these veterinarians were asked to identify client herds in which they suspected BVDV infection based on history and observed clinical signs; these herds were also evaluated for BVDV PI prevalence (52 herds). The prevalence of herds with at least one PI animal in randomly selected herds was 3.9% with a 95% confidence interval (CI) of 1 to 11%, compared to 19.2% of herds with a history of BVDV-compatible syndromes (95% CI of 10 to 33% of herds) (Table 2).[45]

Table 2. Prevalence estimate and 95% Confidence Interval for the presence of at least one PI animal in both randomly selected and BVDV-suspected herds.[45]

	No. Herds Tested	No. Positive Herds	Prevalence Estimate (%)	95% CI (%)
Randomly selected (Low Risk)	76	3	3.9	1-11
BVDV suspect (High Risk)	52	10	19.2	10-33
Total herds	128	13		

Multiple positive calves in 10 (77%) of 13 herds
Range of 1 to 13 positive calves in a herd

One procedure for screening herds for PI cattle prior to the start of the breeding season involves initially testing all replacement heifers and bulls, all calves, and all dams without calves due to calf death or failure to calve.[27] In subsequent years, a strategy of vaccination and herd isolation

from the start of the breeding season until four months after the end of the breeding season to decrease the risk of exposure to animals acutely infected with BVDV should be implemented. For one or more years immediately following the initial whole-herd screening, testing of all calves prior to the start of the breeding season may be required to eliminate PI animals from the herd. Once the herd is free of PI calves and cows, only replacement breeding animals need to be tested for persistent infection with BVDV. Therefore the cost of a BVD PI screening program is high in the initial one to three years, and then lower in following years.

Larson *et al*., showed that at the low prevalence of herds with at least one PI animal reported for randomly selected herds, the dollars available to remove PI animals may or may not justify whole-herd diagnostic screening. If the true prevalence of herds with at least one PI animal is 1% (at the low end of the 95% confidence interval),[45] the average annual dollars available for screening is only $0.15 (Table 3). Using a ten-year period, if all the calves and dams without calves are tested the initial year, the cost of the initial screening is prorated over 10 years, and only replacements (at the rate of 15% of the mature herd) are screened in subsequent years, $0.60 would be available for costs associated with each animal tested (Table 4). This indicates that the cost of screening exceeds the risk of economic loss if the herd prevalence for PI presence is 1%. A strategy to implement a BVDV biosecurity program for incoming cattle (including PI screening) and to maintain a BVDV vaccination program appears to be a better economic alternative compared to whole herd screening for PI animals when history does not indicate problems suggestive of BVDV.

If, however, the true prevalence of randomly selected herds with at least one PI animal is 11% (at the high end of the 95% confidence interval),[45] an average of $1.69 per cow annually is available for the cost of screening the breeding herd (Table 3). This may justify a strategy where all the calves are screened the initial year and replacements are screened in subsequent years in random herds. In such a scenario, if the cost of the initial screening is prorated over 10 years and the herd has a 15% replacement rate, $6.76 would be available for each animal tested (Table 4). This amount may cover the labor, diagnostic laboratory and consulting fees required to initiate a screening protocol.

The economic conclusion is the same if BVDV also affects pre-weaning mortality and weaning weight to a similar extent as modeled, assuming that the cost of initial screening is prorated over 10 years. The dollars available to screen herds for the presence of PI cattle only increases to $0.80 per test if the prevalence of herds with at least one PI calf is 1%. If the prevalence is 11%, the dollars available per animal tested is $8.88 (Table 4).

By pre-screening herds based on a history of BVDV-compatible problems or positive laboratory tests so that the prevalence of herds tested with at least one PI calf increases to 10% to 30%, the economic reward from identifying and removing PI animals is likely to exceed the cost of the presence of PI animals. If the true prevalence of herds with at least one PI animal is 10%, at the low end of the 95% confidence interval reported by Wittum *et al*,[45] the average annual dollars available for screening is $1.53 (Table 3). If all the calves and dams without calves are tested the initial year, the cost of the initial screening is prorated over 10 years, and replacements (at the rate of 15% of the mature herd) are screened in subsequent years, $6.12 would be available for each animal tested (Table 4).

If, however, the true prevalence of herds with at least one PI animal is 30% (at the high end of the 95% confidence interval),[45] an average of $4.60 per cow is available annually to screen the breeding herd (Table 3). This would probably justify a strategy whereby all calves are screened the initial year and replacements are screened in subsequent years. In such a scenario, if the cost of the initial screening is prorated over 10 years and the herd has a 15% replacement rate, $18.40 would be available for each animal tested (Table 4).

If BVDV also affects pre-weaning mortality and weaning weight to a similar extent as was modeled, and the same proration of diagnostic test costs is applied, the dollars available to screen herds with a history of BVDV-compatible problems for the presence of PI cattle increases to $8.08 per test if the prevalence of herds with at least one PI calf is 10% (Table 4). If the prevalence is 30%, the dollars available per test is $24.20 (Table 4).

Table 3. Average annual value of testing to remove PI cattle from the herd (per cow exposed for breeding) (Adapted from Larson *et al*., 2002)

	Herd prevalence of at least one PI animal	10 Year average value of testing to remove PI cattle per cow exposed for breeding
Reproductive effect only		
Randomly Selected Herds	1%	$0.15
	11%	$1.69
BVDV PI Suspect Herds	10%	$1.53
	30%	$4.60
Reproductive and calf mortality effects		
Randomly Selected Herds	1%	$0.20
	11%	$2.22
BVDV PI Suspect Herds	10%	$2.02
	30%	$6.05

Table 4. Dollars available for testing if whole herd screening is done for one year and in subsequent years only replacement animals are screened (per animal tested per year) over a 10-year horizon

	Herd prevalence of at least one PI animal	Dollars available for testing per animal tested per year
Reproductive effect only		
Randomly Selected Herds	1%	$0.60
	11%	$6.76
BVDV PI Suspect Herds	10%	$6.12
	30%	$18.40
Reproductive and calf mortality effects		
Randomly Selected Herds	1%	$0.80
	11%	$8.88
BVDV PI Suspect Herds	10%	$8.08
	30%	$24.20

Conclusions

The cost of initiating a BVD PI whole-herd screening protocol on a farm or ranch is significant. Because of the low prevalence of herds with at least one PI animal, veterinary practitioners may not be economically justified to initiate diagnostic whole-herd screening protocols for PI BVDV cattle for all their clients. Wittum *et al* found that among herds where practitioners suspected BVDV-induced syndromes, 19.2% were found to have at least one PI animal present upon screening (95% CI, 10-30%).[45] By using herd history to pre-select herds that are more likely to benefit from a diagnostic screening protocol for BVDV PI animals, veterinarians can provide a diagnostic and consulting service to their clients that is justified economically. In pre-selected herds, the cost of diagnostic testing is less than the risk of BVDV PI cattle and their cost to herd profitability. In contrast, the cost of diagnostic testing is not likely to be recouped if testing all herds in a general population.

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