

BVDV Management: BVDV Surveillance

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Abstract

Bovine viral diarrhoea virus (BVDV) control programs should include identification and removal of the BVDV persistently infected (PI) animal, biosecurity, biocontainment and surveillance. Surveillance of BVDV in herds previously identified as having persistently infected animals and for herds of unknown BVDV status are the focus of this discussion. Issues discussed are considerations for tests used in BVDV surveillance programs, population for surveillance and timing of testing.

Résumé

Les programmes de lutte contre le virus de la diarrhée virale bovine (BVDV) devraient inclure l'identification et le retrait des animaux infectés permanents immunotolérants (IPI), la biosécurité, le bioconfinement et la surveillance. Le présent exposé porte principalement sur la surveillance du BVDV dans des troupeaux où on a précédemment décelé des animaux infectés permanents immunotolérants (IPI) et dans des troupeaux où la présence du BVDV n'a pas été établie. Parmi les points soulevés, citons les éléments à envisager à l'égard des tests utilisés par les programmes de surveillance du BVDV, les populations à surveiller et le choix du moment pour effectuer les tests voulus.

Introduction

A BVDV eradication and control program should include testing of all suckling calves, open cows, replacement animals, bulls and removal of persistently infected animals, together with a comprehensive biocontainment and biosecurity program to reduce the impact of introduction of the virus. Despite recommendations and best intentions, many producers probably institute partial testing, biocontainment and biosecurity programs, increasing the possibility that BVDV is not eliminated from the herd or may be reintroduced. Therefore, BVDV surveillance programs should be incorporated into herds for timely detection of incomplete elimination or reintroduction. In herds with unknown BVDV status, a BVDV surveillance program could be used to detect introduction of the disease sooner.

Background on Need for Surveillance Programs

An enormous amount has been written about BVDV control and management in recent years, and excellent review articles of disease epidemiology, pathogenesis, clinical signs and control are readily available.^{6,13-15} For BVDV positive herds, these programs are based on the principles of identification and disposal of persistently infected animals, combined with comprehensive biocontainment and biosecurity programs.²⁴ Biosecurity refers to actions taken to prevent introduction of a pathogen, while biocontainment refers to actions taken to control an existing pathogen in the herd.²⁴ There appears to be general agreement that although vaccines can offer some protection against fetal infection, vaccination programs alone are currently unlikely to consistently control BVDV because protection against fetal infection is not 100%.^{2,4,19} For negative herds or herds of unknown BVDV status, biosecurity and biocontainment recommendations remain the same.^{12-14,22} These control recommendations are based on the understanding that BVDV is an infectious disease with the major route of transmission being animal-to-animal contact with excretion and secretions of tears, milk, saliva, urine, feces, nasal discharge and semen, and that a minor portion of transmission may occur due to iatrogenic, fomite, environmental and insect transmission.²³ However, a component of BVDV control programs often given little discussion is surveillance programs for BVDV detection. Because of the wealth of information available on the first three components, the remaining discussion concentrates on justification and implementation of surveillance programs for BVDV in cow-calf herds, a frequently forgotten component of BVDV control programs.

Justification for BVDV Surveillance Program

Control programs based on testing and removing persistently infected animals, biosecurity and biocontainment have been successful at controlling the disease in Europe.¹⁷ However, regions with a high seroprevalence (unvaccinated animals) and high cattle densities have experienced reintroduction of BVDV from outside herds, suggesting that simple removal of animals persistently infected is insufficient to maintain nega-

tive BVDV status.⁸ Another explanation for repeated identification of BVDV in the herd may be reintroduction due to inability to control external forces introducing BVDV into the herd. Reintroduction of BVDV has been documented in high density, high seroprevalence regions of Europe.⁸ For example, investigations in Denmark of 67 previously BVDV-free herds reported prevalence of the following risk factors in those herds: persistently infected animals had been present on adjacent properties (36%), reintroduction was purchased or pregnant animals carrying persistently infected calves (28%), use of common pastures (7%) and persistently infected animal on neighboring farm (3%).¹ Obvious explanations of the remaining 26% of the herds were not identified.¹

These data suggest that BVDV programs should have four components: an initial eradication program (test and remove component) and a control program with three components: biosecurity, biocontainment and surveillance. Surveillance programs for BVDV are required because herds diagnosed with BVDV may fail to eradicate BVDV or eliminate the risk of reintroduction. In 2006, Iowa State University conducted a study of BVDV prevalence in over 12,000 spring-born calves from 102 cow-calf herds in Iowa.²⁷ Only calves born in the spring of 2006 were tested, as these were likely the most sensitive subset population to detect BVDV in those herds. The calves were tested for BVDV using antigen capture ELISA (ACE) on ear notches (skin). A component of the study evaluated risk factors for detection of BVDV in the calves.

Eleven of 102 herds tested positive for BVDV based on ACE from ear notches collected from calves. Six of these 11 BVDV positive herds indicated that BVDV had been diagnosed in the herd prior to enrollment in the study. Low adoption of, or compliance with, BVDV eradication programs may explain repeated identification of BVDV in these herds. To evaluate these possibilities, a phone survey of 50 veterinarians with clients' herds diagnosed with BVDV using immunohistochemistry (IHC), from August 2006 to March 2007, was conducted. Veterinarians were asked to recall the testing, vaccination and general biosecurity programs they recommended to the client (Table 1). Producers were asked the same questions, reframed to refer to the instructions given to them by their veterinarians. Further, veterinarians and producers were asked if instructions for program changes were in the form of 1) a pamphlet about BVDV control, 2) veterinarian-written instructions pertaining to the producer's individual situation, 3) verbal instructions, or 4) other instructions.

Of 50 veterinarians interviewed, 46 agreed to be interviewed and 28 identified their clients as raising cattle for beef. Of the 28 veterinarians that worked with beef clients, 27 responded that they had recommended to either test some animals, change vaccination practices and/or change biosecurity practices.

Veterinarians frequently recommended full testing programs, with changes in type and/or frequency of vaccination and biosecurity practices (nine of 28 programs).

Table 1. Questions for survey.

Questionnaire area	Specific questions
Testing program	1) whole-herd testing (yes/no) 2) testing of dams of positive animals (yes/no) 3) testing of calves (yes/no) 4) testing of heifers (yes/no) 5) testing of bulls (yes/no) 6) other testing (open)
Vaccination program	7) changing the modified-live vaccine (yes/no) 8) changing the type of killed vaccine (yes/no) 9) changing from killed to modified-live vaccines (yes/no) 10) other changes (open)
Biosecurity programs (other than vaccination)	11) changes in the biosecurity practices (yes/no) 12) testing for infected animals before they enter the herd (yes/no) 13) isolating newly purchased animals for 14-21 days (yes/no) 14) purchasing replacement animals from a known source (yes/no) 15) restricting the movement of sick cattle (yes/no) 16) cleaning and sanitizing all working facilities and equipment (yes/no) 17) after handling cattle with chronic diarrhea or severe illness (yes/no) 18) monitoring fence-line contact of animals during grazing (yes/no) 19) avoid contact with animals of unknown health status (yes/no) 20) not allowing the fecal material from scouring animals to contaminate other animals or humans (yes/no) 21) changes in cattle showing practices (yes/no) 22) other recommendations (open)

In 10 programs, no testing was recommended— a proportion of these programs may have been from feedlot producers. Of producers interviewed, 25 identified themselves as beef producers—either cow-calf, feedlot or cow-calf and feedlot. Only four producers recalled being advised to test the entire herd, while 16 recalled being advised to test a partial group of the herd. Eleven producers recalled being advised to change the type and/or frequency of vaccination. Twelve producers recalled being advised to change biosecurity practices.

For all 46 veterinarians who participated in the survey (dairy and beef clients), 38 indicated they gave verbal instructions to clients to control BVDV programs, and only 12 indicated they had provided written instructions for the control program. Interestingly, of 34 producers diagnosed with BVDV (dairy and beef), only 24 indicated they received verbal instruction on carrying out a BVDV control program and only six producers indicated they had received verbal and written instructions on implementing the programs. Further, in a survey of laboratories testing for BVDV, only 55% provided information about BVDV management.⁵

These data suggest that producers are either being advised to use partial testing programs or failing to understand BVDV control programs. Both options increase potential for reintroduction of BVDV due to inadequate biosecurity and biocontainment or failure to eradicate BVDV from the herd after initial diagnosis.

In summary, herds with BVDV may fail to eliminate the virus and continue to suffer production losses due to infection if the control program is not properly instituted. Surveillance programs aid in detection and early correction of control program failures. Given the estimated cost of BVDV infection in a herd ranges from \$14.85 to \$24.84 per animal, a low cost surveillance program that detects reintroduction or failure to eradicate BVDV should be an essential component of any control program.¹⁶

What are the Components of a BVDV Surveillance Program?

Surveillance programs are generally designed for units of concern much larger than the herd, i.e. the region or the country. However, all infectious disease surveillance programs aim to detect the presence of the organism using a cheap, convenient and accurate method. All surveillance programs require a compromise between accuracy and cost. The cheapest and most convenient surveillance program for BVDV is examination of records for changes in production indicative of BVDV. However, this approach appears to be inaccurate. In studies of herds with no clinical evidence of BVDV, 10 of 19 herds were subsequently found to be BVDV positive,⁹ while 42 of 52 herds suspected to be BVDV positive were PI nega-

tive.²⁸ Therefore, programs that include testing for presence of the virus in the herd are needed. Unfortunately, apart from pooled sera there are no clear estimates of sensitivity and specificity of BVDV surveillance programs. Therefore, veterinarians will need to use knowledge of the epidemiology and management of the herd to recommend the best surveillance programs. A surveillance program for a cow-calf herd with BVDV should consider three components:

- Test and tissue
- Target population
- Timing of collection

What Test and Tissue Should be Used in a BVDV Surveillance Program?

Many surveillance programs begin with a decision about detecting infection (antigen) or exposure (antibody), however, as vaccination is currently a fundamental recommendation of BVDV control programs in North America, testing for exposure is not discussed further.

Given that the program will be based on detection of infection, the next step is to decide the test and sample to use. The choice of test and sample are entwined, as some tests are available for some sample types. For individual animal testing to detect the presence of infection using either immunohistochemistry (IHC), ACE, virus isolation or PCR are readily available.⁵ All these tests are considered to have high sensitivity and specificity for acutely infected calves, and are therefore good choices for BVDV surveillance programs aimed at detecting presence of the virus in the herd.³ As comparisons of the tests show very little difference, it would appear that cost and convenience should drive the decision about the test used in surveillance programs.^{3,7} Virus isolation and PCR tend to be more expensive on an individual test basis; therefore, IHC and ACE are the remaining options if the herd owner decides to use individual animals. The next factor is convenience of sample collection. Blood samples required for ACE on sera may incur increased labor for bleeding, a cost not incurred if the tissue used is an ear notch sample. Ear notches can be tested using ACE and IHC, and the laboratory should be contacted about price and turnaround for each test.

An alternative to individual testing is pooling of samples, which decreases the cost of surveillance. Pooling by its nature must decrease the sensitivity of a testing system; however, for some individual samples the amount of virus is so high that the sensitivity in pooled samples remains acceptably high. Further, there needs to be a balance in number of animals per pool and likelihood of positive samples, as positive pools eventually need to be broken out to individual positive samples. As an extreme example, combining all samples into a single pool for a known positive herd would increase the cost of test-

ing, as the producer would be required to pay for pool testing followed by individual tests for all animals in the pool.

For BVDV testing programs, pooled samples are usually tested with PCR technology.⁶ It is important to differentiate which samples are being pooled when discussing practicality and sensitivity. Pooled milk samples are not practical for beef producers and will not be discussed further. Pooled sera samples are highly sensitive.²⁶ The advantages of pooling sera are greater when the prevalence of persistently infected animals is low, because then the majority of pools are negative. In a comparison of five pooling protocols, the benefits of pooling decreased above a prevalence of 3% persistently infected animals, assuming 100% sensitivity and specificity of the pooled PCR. The benefits of pooling are also associated with the number of samples that can be included in an individual pool. Some laboratories may suggest smaller pool sizes due to concerns about sensitivity.^{20,21} The disadvantage of pooled sera is the cost of labor associated with sample collection, so there has been interest in testing pooled ear notches using PCR. Pooled ear notches have been reported as a sensitive method of detecting persistently infected cattle and this testing is currently offered by several laboratories.^{10,11} The approach is relatively new, and unpublished accounts suggest some laboratories have been unable to consistently detect the presence of BVDV in pools. Therefore, until more published studies are available it would be best to work directly with the veterinary laboratory and inquire about protocols used to assess the pooling process. Pooled assays should be assessed using blinded field samples as well as laboratory created pools.

Who Would Be Tested in a Surveillance Program?

There are three approaches to animals tested in a surveillance program: 1) the whole herd, 2) a random sample of the herd, and 3) a risk-based sample of the herd. Further, the choice of study population is intertwined with the choice of sample and test, as some samples, tests and units of concern are only applicable to some subsets. A whole-herd test as a surveillance program could be based on individual tests or pooled PCR on sera. For example, a surveillance program could initially test all animals on the herd in pools: suckling calves, cows without tested calves, heifers and bulls. In subsequent years, only animals that are new to the herd (purchased bulls, replacement heifers and cows) and calves need to be included in the sample. Another option is individual testing of all animals as described above using IHC or ACE. Testing the whole population increases the herd level sensitivity of the surveillance program, but also increases the cost of the surveillance program.

In veterinary surveillance, many programs are

based on a random sample of the population. This might be thought of as statistical surveillance: testing based on the probability of detecting an animal positive, based on the prevalence of positive animals in the herd. Using commonly available tables, the number of animals to be sampled based on an expected prevalence, sensitivity and specificity and desired level of confidence are determined.¹⁸ Surveillance systems based on random sampling, however, are only ideal when the outcome being measured is common and there is no information on the epidemiology of the disease or risk factors for exposure. As the presence of infection with BVDV (i.e., the presence of antigen) is a rare event in most herds (< 1%), a randomly based program would require testing of all animals, and therefore is not sensible. Random sampling surveillance could be used in herds without vaccines to detect antibodies which should be common post-exposure, however, this is not recommended as vaccination is an integral part of the BVDV control program in the USA and would interfere with interpretation of the data.²⁵

Finally, risk-based surveillance systems may be used solely or combined with a whole-herd program described above. A risk-based surveillance program is based on the epidemiology of the disease. A risk-based system should utilize samples collected from those animals most likely to have BVDV if present in the herd, to maximize the sensitivity of the program. For many herds, a risk-based system would collect samples from all neonatal and post-natal deaths, ill neonates, as well as abortions. Further, during unusual outbreaks of disease in young animals, samples should be collected and tested routinely. Obviously the combination of a risk-based surveillance program and routine whole-herd programs are more effective at detecting the introduction of BVDV, and more expensive.

Collection of samples for risk-based surveillance should be routine and convenient. Producers could be instructed to collect a skin sample from all dead animals. Although not ideal, these could be stored in a freezer until the next veterinary visit or sufficient samples have been collected, and then submitted to the laboratory. Again, although not ideal the samples can be stored in a freezer until submission is convenient.

Timing of Sample Collection

Timing of risk-based surveillance samples is not an issue, as samples would be collected as cases occur. However, collection of whole herd samples or subgroup samples from well animals should be timed to occur in a window of opportunity that would allow animals to be removed from the herd before breeding occurs, i.e. collect samples from calves as born, and open cows that do not calve, replacement heifers and bulls before breeding begins. A sensitive, but more expensive, surveillance pro-

gram could collect samples from all calves at birth and open cows. Another subgroup that could be targeted is calves at weaning, when it is convenient to collect ear notch samples. However, because persistently infected calves may have lived long enough to transmit the virus to pregnant cows but died before weaning, this approach will not be as sensitive as testing calves at birth.

Obviously, a large number of herds do not have a window of time when no pregnant animals are in the herd, due to extended breeding seasons or distinct fall and spring calving seasons. In these herds, the same animals should be included in the program. However, this program will be less effective at detecting a BVDV incursion, as pregnant animals may be present and harboring the disease.

Conclusions

Given the incomplete nature of some BVDV control programs and the possibility of reintroduction of BVDV, herds diagnosed with the disease should adopt a BVDV surveillance system as well as a comprehensive biocontainment and biosecurity program after disease eradication. To design a BVDV surveillance program, veterinarians need to work with producers on the costs and benefits of the program. When designing a program consider the impact of the tests, the population tested and the timing of testing on the sensitivity of the surveillance program.

References

- Bitsch V, Hansen KE, Ronsholt L: Experiences from the Danish programme for eradication of bovine virus diarrhoea (BVD) 1994-1998 with special reference to legislation and causes of infection. *Vet Microbiol* 77:137-143, 2000.
- Brock KV, Cortese VS: Experimental fetal challenge using type II bovine viral diarrhoea virus in cattle vaccinated with modified-live vaccine. *Vet Therapeutics* 2:354-360.
- Cornish TE, van Olphen AL, Cavender JL, Edwards JM, Jaeger PT, Vieyra LL, Woodard LF, Miller DR, O'Toole D: Comparison of ear notch immunohistochemistry, ear notch antigen-capture ELISA, and buffy coat virus isolation for detection of calves persistently infected with bovine viral diarrhoea virus. *J Vet Diagn Invest* 17:110-117, 2005.
- Cortese VS, Grooms DL, Ellis J, Bolin SR, Ridpath JF, Brock KV: Protection of pregnant cattle and their fetuses against infection with bovine viral diarrhoea virus type 1 by use of a modified-live virus vaccine. *Am J Vet Res* 59:1409-1413, 1998.
- Driskell EA, Ridpath JF: A survey of bovine viral diarrhoea virus testing in diagnostic laboratories in the United States from 2004 to 2005. *J Vet Diagn Invest* 18:600-605, 2006.
- Goyal SM: Diagnosis, in: Goyal SM, Ridpath JF (eds): *Bovine Viral Diarrhoea Virus. Diagnosis, Management and Control*, ed 1. Ames, Blackwell Publishing Ltd, 2005.
- Hilbe M, Stalder H, Peterhans E, Haessig M, Nussbaumer M, Egli C, Schelp C, Zlinszky K, Ehrensperger F: Comparison of five diagnostic methods for detecting bovine viral diarrhoea virus infection in calves. *J Vet Diagn Invest* 19:28-34, 2007.
- Houe H: Risk Assessment, in: Goyal SM, Ridpath JF (eds): *Bovine Viral Diarrhoea Virus. Diagnosis, Management and Control*, ed 1. Ames, Blackwell Publishing Ltd, 2005.
- Houe HMA: Prevalence of bovine virus diarrhoea (BVD) in 19 Danish dairy herds and estimation of incidence of infection in early pregnancy. *Prev Vet Med* 11:9-16, 1991.
- Kennedy JA: Diagnostic efficacy of a reverse transcriptase-polymerase chain reaction assay to screen cattle for persistent bovine viral diarrhoea virus infection. *J Am Vet Med Assoc* 229:1472-1474, 2006.
- Kennedy JA, Mortimer RG, Powers B: Reverse transcription-polymerase chain reaction on pooled samples to detect bovine viral diarrhoea virus by using fresh ear-notch-sample supernatants. *J Vet Diagn Invest* 18:89-93, 2006.
- Larson RL: Management systems and control programs, in: Goyal SM, Ridpath JF (eds): *Bovine Viral Diarrhoea Virus. Diagnosis, Management and Control*, ed 1. Ames, Blackwell Publishing Ltd, 2005.
- Larson RL, Grotelueschen DM, Brock KV, Dargatz DA, Ellis JA, Hunsaker BD, Lewis SD, MacGregor DS, Smith RA, Sprowls RW, Traffas V: BVD decision/management guidelines for beef veterinarians. *Bov Pract* 38:103-112, 2004.
- Larson RL, Grotelueschen DM, Brock KV, Hunsaker BD, Smith RA, Sprowls RW, MacGregor DS, Loneragan GH, Dargatz DA: Bovine viral diarrhoea (BVD): review for beef cattle veterinarians. *Bov Pract* 38:93-102, 2004.
- Larson RL, Miller RB, Kleiboeker SB, Miller MA, White BJ: Economic costs associated with two testing strategies for screening feeder calves for persistent infection with bovine viral diarrhoea virus. *J Am Vet Med Assoc* 226:249-254, 2005.
- Larson RL, Pierce VL, Grotelueschen DM, Wittum TE: Economic evaluation of beef cowherd screening for cattle persistently-infected with bovine viral diarrhoea virus. *Bov Pract* 36:106-112, 2002.
- Lindberg A, Alenius S: Principles for eradication of bovine viral diarrhoea virus (BVDV) infections in cattle populations. *Vet Micro* 64:197-222, 1999.
- Martin SW, Meek AH, Willeberg P: *Veterinary Epidemiology: Principles and Methods*. Ames, Iowa State University Press, 1987.
- Moennig V, Eicken K, Flebbe U, Frey HR, Grummer B, Haas L, Greiser-Wilke I, Liess B: Implementation of two-step vaccination in the control of bovine viral diarrhoea (BVD). *Prev Vet Med* 72:109-114, 2005.
- Munoz-Zanzi C, Thurmond M, Hietala S, Johnson W: Factors affecting sensitivity and specificity of pooled-sample testing for diagnosis of low prevalence infections. *Prev Vet Med* 74:309-322, 2006.
- Munoz-Zanzi CA, Johnson WO, Thurmond MC, Hietala SK: Pooled-sample testing as a herd-screening tool for detection of bovine viral diarrhoea virus persistently infected cattle. *J Vet Diagn Invest* 12:195-203, 2000.
- Smith DR, Grotelueschen DM: Biosecurity and biocontainment of bovine viral diarrhoea virus. *Vet Clin North Am Food Anim Pract* 20:131-149, 2004.
- Thurmond M: Virus transmission, in: Goyal SM, Ridpath JF (eds): *Bovine Viral Diarrhoea Virus. Diagnosis, Management and Control*, ed 1. Ames, Blackwell Publishing Ltd, 2005.
- Tremblay R: Choosing a new vaccine: a solution or a potential problem. *Proc Am Assoc Bov Pract* 36:58-62, 2005.
- Waldner CL, Campbell JR: Use of serologic evaluation for antibodies against bovine viral diarrhoea virus for detection of persistently infected calves in beef herds. *Am J Vet Res* 66:825-834, 2005.
- Weinstock D, Bhudevi B, Castro AE: Single-tube single-enzyme reverse transcriptase PCR assay for detection of bovine viral diarrhoea virus in pooled bovine serum. *J Clin Micro* 39:343-346, 2001.
- Whipple AE, Kinyon JM, O'Connor A.M.: The association between putative causal organisms and the occurrence of infectious bovine keratoconjunctivitis in beef calves. *Proc 85th Conf of Research Workers in Animal Diseases*, p 107 (Abstract), 2004.
- Wittum TE, Grotelueschen DM, Brock KV, Kvasnicka WG, Floyd JG, Kelling CL, Odde KG: Persistent bovine viral diarrhoea virus infection in US beef herds. *Prev Vet Med* 49:83-94, 2001.