Control of BVDV: Keep it Simple, Vaccinate, and Pay Strict Attention to Heifer Management

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Abstract

Much progress had been made in defining BVDV in molecular terms. While this information has been useful in some aspects of BVDV pathogenesis, this information has not led to a significant decrease in concern expressed by practitioners regarding prevention and control of BVDV-induced disease. There are several factors which contribute to this continued uneasiness, but a major contributor may be the inability of research personnel to deliver a clear and concise message concerning BVDV. The most important aspect of control of BVDV is the prevention of the generation of persistently infected animals. Management is a significant factor and the management of heifers may be the most overlooked problem in BVDV control programs.

Nine years ago, I addressed the AABP convention in Buffalo on the role of persistently infected animals in cases of fatal BVDV-induced disease. As I look back over the intervening nine years, I am impressed by the great strides that we have made in the area of the molecular biology of BVDV. We have a large number of monoclonal antibodies specific for BVDV which can detect minor differences in the various isolates of the virus. We have defined the proteins encoded by the BVDV genome and we know the complete nucleotide sequence of several BVDV isolates. The relationship among the isolates of hog cholera virus, BVDV, and border disease virus is being determined from an evolutionary standpoint. It is clear that cytopathic strains of BVDV arise as mutations of the noncytopathic strains and that biotype and antigenicity are independent variables. Finally, we are comfortable with the proposed mechanism for the induction of mucosal disease, i.e. a persistently infected animal being challenged with a cytopathic variant which replicates in an enhanced manner sufficient to produce a fatal outcome. Yet, in spite of all of these advances, I do not see much change in the questions being asked by practitioners concerning control and prevention of BVDV. Why?

We can certainly blame the virus for the some of confusion that continues to exist. The various clinical manifestations of a BVDV infection are remarkably varied from the subclinical to the rapidly fatal infections recently encountered in Canada. Whether this represents a new more virulent strain of BVDV is open for debate. Even in the subclinical events, reproductive dysfunctions can occur which may not be temporally related to an infection, but which can have significant ramifications at a later date. This aspect will be discussed later.

Diagnostic laboratories also add to the confusion by their inability to consistently diagnose BVDV infections. Poor diagnostic reagents and the ubiquitous presence of noncytopathic BVDV in fetal bovine serum has led to inconsistent laboratory data. With the introduction of vaccines, the picture of BVDV seems to have changed from a herd outbreak problem to one of a more chronic nature. The chronic form of the problem is even more difficult to diagnose because of the limited number of animals involved in any given clinical episode.

Part of the confusion may also rest with those who were engaged in BVDV research. The earliest isolates of BVDV were noncytopathic in nature, i.e. they did not produce overt cytopathology *in vivo*. However, these viruses did kill cows and cause reproduction dysfunctions. With the isolation of cytopathic strains of BVDV, most laboratory workers shifted to these viruses, because they were easier to manipulate in the laboratory. Thereafter, most *in vivo* studies were conducted using cytopathic strains of BVDV and the resulting clinical events were ascribed to cytopathic BVDV. Many practitioners trained in the 70's and early 80's did not believe that BVDV infections were a problem and if they were, the cytopathic strains were the culprit. One could ignore noncytopathic BVDV.

The issue of mucosal disease also seems to have mesmerized a large number of BVDV researchers. Most of the literature on the pathology of BVDV is on mucosal disease. It is a wonderful disease from the perspective of the pathologist because of the overt lesions that one can describe. It was a challenging disease because of its sporadic nature and the elucidation of the mechanism for the production of this disease was a remarkable finding. There is perhaps no other viral disease with such a unique pathogenesis. However, the economic impact of mucosal disease for the bovine industry is at best minimal.

Practitioners are still confused as to the efficacy of

BVDV vaccines. In the area of preventing the generation of PI animals, the biologics industry along with the USDA appear to have been "asleep at the switch". The definitive study as to the production of PI animals was published in 1984. There were already strong indications that BVDV vaccines were not consistently preventing the production of PI animals. Requests for more research dealing with vaccine efficacy and fetal protection were largely ignored. There is no doubt that these studies would be very expensive, but if BVDV is to be controlled, the practitioner must have information of the degree of fetal protection afforded by the commercial products.

The challenge which is still with us nearly 50 years after the first clinical descriptions of BVDV infections in cattle is to develop effective means to control BVDV infections. To do this, the practitioner must be able to deliver a clear, concise, and consistent message to the producer. This message must include a simple description of the pathogenesis of BVDV, the role management plays in this problem, and the limitations of vaccines in the context of the producer's management philosophy.

To develop a clear and concise story about BVDV, the practitioner might be better off if he forgot or ignored a few things. First, one should forget that they have ever heard of cytopathic BVDV. We can eradicate BVDV without ever recognizing the existence of cytopathic BVDV. For every cytopathic BVDV, there is a noncytopathic BVDV with the identical antigenic structure since cytopathic BVDV arises as a mutant of noncytopathic BVDV. Therefore, there is nothing unique about the antigens of cytopathic BVDV. Cytopathic BVDV cannot maintain itself for long in the bovine population and once all susceptible animals in a herd have been infected, it will disappear. Noncytopathic BVDV can produce all of the clinical manifestations ascribed to cytopathic BVDV, but in addition, noncytopathic BVDV produces persistently infected animals which is the key for survival of BVDV in the bovine population.

The practitioner would in reality be advised to ignore most of the information published concerning mucosal disease. As indicated previously, its contribution to economic losses caused by BVDV are negligible. The only aspect of mucosal disease which must be remembered is that the heart of the problem is a persistently infected animal. There are also a number of publications which attempt to describe the immunological deficits of the persistently infected animals. While these data may be interesting for researchers, for the practitioner, this information is also irrelevant. The PI animal cannot be "saved" and to keep these animals in a herd is economic suicide. For the owner, the consistent message must be that the PI animal should be identified, eliminated, and prevented from re-emerging in the herd.

What are the elements of the clear and concise story regarding BVDV? For the dairy industry, BVDV should be considered first and foremost a reproduction problem and most of the economic consequences of BVDV infections are a result of reproductive dysfunction. This being the case, control of BVDV must take into account the reproductive status of the animals on the farm and those that are entering the production unit. Control of BVDV will require a vaccine program that must be integrated with the management style of the producer. Currently, there is no vaccine program that fits all management philosophies.

The consequences of a BVDV infection depends on the immune status of the cow, the strain of the virus, and the gestational stage of the cow. For the unprotected cow, infection with BVDV from the time of breeding up to approximately 30 days post breeding can result in the death of the embryo. Recent data dealing with this early period of the reproductive cycle indicates that embryonic losses may reach 50%. Clearly, some repeat breeding problems can be related to acute BVDV infections. With vaccinated animals, the number of affected animals may be significantly diminished so that the problem presents itself in a somewhat sporadic fashion, making a diagnosis very difficult.

The most important gestation period with regard to the control of BVDV is the period between 40 and 120 days. It is during this time period that BVDV gains access to the fetus and can establish a persistent infection. This can occur because the fetus does not have an immune system that is sufficiently mature to recognize BVDV as a foreign antigen. Cytopathic BVDV will kill the fetus at this stage while noncytopathic BVDV can either kill the fetus or establish the persistent infection. Abortions are certainly economic losses at this stage, but long term problems do not develop from abortions. The birth of a persistently infected animal can insure the continued presence of BVDV in the herd and the establishment of chronic BVDV problems.

Infection of a fetus after 120 days gestation will not result in a persistently infected fetus because the fetus is now able to respond immunologically to the BVDV antigens. Abortions and congenital malformations can be the consequence of BVDV infections up to about 180 days gestation. Beyond this period of time, the fetus may abort, but there appears to be no developmental repercussions of the infection if the fetus survives to term. A fetus infected with BVDV after 120 days gestation will be born with an active immunity to BVDV and will have a positive antibody titer to BVDV in a precolostral sample. The loss of a calf through an abortion or because of congenital problems is significant, but the seeds of future problems have not been sown because PI animals have not been produced.

The message for controlling BVDV is relatively simple; keep the virus from reaching the fetus. If virus

does not reach the fetus before 120 days gestation, then PI animals cannot be produced. One might ask that if controlling BVDV is conceptually relatively simple, why is BVDV still a problem. The simple answer is that theory is not translated well into practice and there are areas of special concern that are ignored or judged too inconvenient. I will address some of these areas, but one additional point needs to be stressed concerning PI animals. The vast majority of PI animals come from normal immunocompetent dams. There are instances of a PI animal surviving long enough to produce a PI calf, but these are very rare in the commercial dairy industry of the US and Canada. PI calves are produced because the dam does not have adequate immunological protection against BVDV.

Obviously, if the producer chooses not to vaccinate for BVDV, then all cows in the unit may be fully susceptible to BVDV and a classic herd outbreak may occur with variable mortality in all ages of animals, abortions, defective calves, and the production of persistently infected calves. The losses in this situation may be severe enough to force a closure of the production unit. This situation has occurred recently in Canada with significant economic losses.

Most dairy farmers in the Northeast vaccinate for BVDV, but problems still persist. In many of these instances, the vaccine program does not match the management philosophy. By that I mean that management practices negate or subvert the vaccine program. There are many instances in which this happens. In some cases, the producer wants the veterinarian to vaccinate all animals at the same time once a year. With this type of program, there will be cows that will have been vaccinated 9-11 months prior to their next breeding cycle. Particularly with regard to killed vaccines, it is generally accepted that fetal protection will be minimal at best when the interval between vaccination and challenge is this great. Vaccination once per year on average can be successful if the producer pays attention to the reproductive status of his animals. Vaccination just prior to breeding ensures maximum protection for the fetus in that critical period when PI animals are produced. This type of vaccination program can be the most economical, but it requires active participation of the producer in either vaccinating the animals himself or scheduling the veterinarian on a routine basis.

If the producer chooses not to think about when this animals should be vaccinated, then the veterinarian should recommend a program of complete herd vaccination at a minimum of twice per year and preferably three times when killed vaccines are administered. The vaccination frequency for modified-live vaccines is still open for debate and more data will be needed to determine the longevity of the protective immunity as it relates to fetal protection.

We now come to the area of herd management which accounts for much of the BVDV problem. This is the area of heifer management. In countless conversations which practitioners concerning BVDV and vaccination, I hear that the heifers were not vaccinated or received only a single does of a killed vaccine prior to breeding. The reasons for this is are numerous, but they all point to poor management. What happens with these animals and vaccination is the exact opposite of what should happen. The five year old animal in a vaccinated herd has had 4-6 doses of vaccine prior to breeding even with a yearly vaccine program. The chances of generating a PI calf in this animals is small. For the heifer with none or one vaccination, the chances are very good that virus will get to the fetus if challenged. Controlling BVDV means paying special attention to the vaccine program for the heifers. Three vaccinations prior to breeding is probably a minimum program for heifers.

A practice which is becoming more common is the purchase of bred heifers. From the standpoint of BVDV, one should consider that when buying bred heifers, one is also buying BVDV unless you have documentation of an adequate vaccination program prior to breeding. Unfortunately, there is no simple test that can be done on the heifer to insure that her fetus is uninfected. The heifer can appear to be the healthiest animal in the herd, but her fetus may contain the virus which starts a chronic BVDV problem in the herd. Some producers have chosen not to keep any calves from these purchased animals as a way to reduce the risk of exposing mature animals in the resident herd. If this is not done, then all calves from these animals should be considered infected until proven otherwise.

In summary, I believe that BVDV can be controlled, but it will take a concerted effort to do so. The question that practitioners should be asking is what is the best vaccination program for this producer rather than what vaccine should I use. The story of BVDV must be demystified for the producer. The French historian and philosopher de Tocqueville said "The Public will believe a simple lie rather than a complex truth." For BVDV, the producer will accept a simple truth rather than a convoluted truth. Keep it simple, vaccinate, and pay attention to the heifers.