Bovine Viral Diarrhea in Dairy and Beef Cattle

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Abstract

The objective of the literature review was to understand the nature and characteristics of BVD within dairy and beef herds. The paper reviewed important aspects of the disease that are relevant and practical to producers. The ideas and opinions presented in the paper were a result of compilation and review of the current literature focused on BVD. Some particular areas of focus were general information about the disease, costs and effects, pathophysiology, virology, transmission, prevention and testing. Information provided throughout the paper attempts to link practices that producers may adopt or modify in order to minimize effects of the disease. A central theme portrayed throughout the paper is that BVD has the potential to be a devastating disease to herds with high numbers of persistently infected animals. Losses from the disease are such due to the broad nature of the virus. Many crucial areas of an operation such as reproduction, weight gain, milk production, and secondary diseases are sectors that cause the most losses to producers. This paper discusses the breadth of the disease as well as the wide spread effects from a clinical and economic level. Even though the disease may seem overwhelming to many producers, minimizing the effects of the virus within a herd may be completed through a few basic practices. This paper attempts to show that the potential for complete eradication of the disease may be possible on a herd and national level. Areas that would benefit from follow up work would be comprehensive economic effects generated from the disease.

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Objective

To understand the nature and characteristics of Bovine Viral Diarrhea (BVD). Emphasis will be placed on knowledge and topics that are practical and applicable for producers, in order to possibly serve as a guide for how to reduce the effects of BVD within a dairy or beef herd.

Introduction

History and Discovery

Bovine Viral Diarrhea continues to be a disease of great importance to dairy and beef producers. The broad nature of the disease, transmittance, and lack of treatment have made BVD a global pandemic, and one of the most significant cattle diseases in the world (Gunn et al., 2005). Coupled with vast clinical symptoms and associated death loss, the gravity of BVD makes it a disease that can no longer be overlooked.

Bovine Viral Diarrhea Virus was first described in New York in 1946 as a disease that mostly affected gastrointestinal tracts of cattle (Olafson, Rickard, 1947). As more became known about the disease, BVD was found to clinically affect multiple other body systems including respiratory and reproductive. At the time, effective prevention methods such as vaccination and testing were unavailable and producers had few options on how to approach the disease. Breakthroughs in research in the 1960's allowed for cell culture-based laboratory assays to detect animals carrying the virus, although the feasibility and ease of these tests were not justified. Regardless of lack of diagnostic

testing, isolation and identification of the virus was possible which led to the practical approach to developing a vaccine capable of mobilizing specific antibodies. The route of active immunity was one of the first preventative measures producers used to fight the disease, and one that is still used today.

Effects

The overall effects of BVD are difficult to examine, due to the breadth of the disease. Research and data highlighting effects of the disease is very limited, simply due to the fact that too many variables are present for accurate measurement. The calculated values of overall economic losses associated with the disease in the U.S. have been compared to those associated with mastitis (Fourichon et al., 2005). Although this may be a rough estimate, there is no debating the substantial monetary amounts linked to the disease. Furthermore, if taken into account the worldwide prevalence of BVD, it is easily understood why be BVD is an important cattle disease from an economic standpoint (Larson et al., 2004).

The areas affected by BVD, specifically, reproduction, production and immunosuppression, are what make it such an expensive disease. Reproductive disorders caused include abortion, early embryonic loss, and fetal defects. Production effects span those regarding decline in feed to gain efficiency, lower carcass quality, and decreased milk production. Finally, immunosuppression may lead to secondary disorders, along with a whole host of other diseases.

General Perception

General perception of the virus has played a large role in fighting the disease from the discovery of BVD to present. In the early stages of research little action was taken against the disease simply due to the fact that not much was known. As the understanding of virology and pathophysiology for the disease increased, more options became available for producers to take advantage of such. But, unfortunately, many producers still chose to overlook and ignore the presence of BVD as a significant bovine disease within their herds. This form of thinking has led to the continued proliferation of the disease within dairy and beef herds across the country.

Advancements and Progress

Research and understanding of BVD within the last 20 years has provided producers with an excess of resources and models on how to limit the disease. With the use of reverse transcription-polymerase chain reaction (RT-PCR) as a means of testing large quantities of animals quickly, producers may now know the BVD status of their herd the same day samples are recovered. The ability to test animals has allowed for effective "test and cull" programs that have decreased the number of positive and carrier animals tremendously. By liberating the herd of these animals, transmission has decreased greatly.

Additionally, with the increased efficacy of vaccines, it has given producers and veterinarians further direction on how to prevent the disease. Research on BVD has pinpointed not only what vaccines to use, but also the timeline of when it is appropriate

and most effective to use them. Possibly the most important advancement made with prevention is the increased knowledge of coupling active immunity along with passive immunity. We now know that it is not a matter of one or the other, yet both used together form a potent barrier against infiltration of the virus.

Acceptance of the disease along with the efforts of veterinary and producer groups to establish BVD control programs, have added to the decrease in ramifications of the disease in North America. Some countries in Europe have even designed national BVD eradication programs aimed at completely eliminating the disease from their country. In the years to come, control and possible eradication of BVD will depend on the will power of producers and veterinarians to take great measures along with unwavering cooperation within the industry.

Costs and Effects

As we have introduced, the effects of BVD are wide-ranging. Because of the vague and diverse clinical signs observed with the disease, it is very difficult to clinically diagnose BVD infected cattle. The difficulty of clinically diagnosing BVD positive cattle impedes the studying of these cattle in a clinical setting. Regardless, understanding the nature of viral infections in animals it should be noted that the side effects are not usually contained to one specific area of the body. A virus such as BVD has been noted to have potential complications with every body system in cattle. Although rare, BVD viruses have manifested in ways as rare as causing skeletal deformities (Spagnuolo, 1997) to severe neurological damage.

As with any other expense added to a producers spreadsheet, the question is always: is the price worth the expense? By raising the question of this cost-benefit analysis, this paper will attempt to explain how the time, effort and resources are well used in decreasing the effects of BVD. In doing this, the paper will focus on the most prevalent clinical effects observed along with additional data highlighting monetary losses associated with the disease.

Reproduction

The topic of reproductive effects in regards to BVD is one of the key areas of focus for producers. Although financial data on overall losses in regards to reproductive inefficiency is unavailable, all literature reviewed ranks reproduction as one of the top factors for total economic loss caused by BVD. This area may also be thought of as a double-edged sword not only from the immediate losses, but also from the perpetuation of the disease to the next generation as well.

Beginning with the subtle yet important reproductive effects caused by BVD, these disorders begin with the overall condition of the animal. As the paper has already discussed, infected animals can be expected to perform below their herdmates. The general, umbrella cause of this is ascribed to overall immunosuppression. This extensively weakened immune system will have negative reproductive effects. When an animal is fighting off any form of disease, the body often compromises the reproductive system in order to sustain other life-essential body systems.

This idea coupled with the likelihood that a lower body condition may be present will affect regular estrous cycles of heifers and cows. Irregular cycling of cattle will

likely lead to lower conception rates in a natural or artificial breeding system. Even if conception rates are not noticeably depressed, the length of breeding season will be affected. Especially when considered in a natural breeding setting, the bull servicing may still get a heifer bred, but if she has not shown heat in previous cycles her conception may be months behind the rest of the herd. An extended breeding season may then lead to culling of beef cows and extended days in milk (DIM) for dairy cattle. In BVD infected dairies, cows open at 150 days or greater was 18.2% higher than dairies with lower BVD infection rates (USDA, 2007). The lengthened breeding season in beef herds and prolonged DIM in dairy herds will cause reproductive inefficiency and therefore overall inefficiency in the operation. Furthermore, increased culling rates from these factors will cause producers to purchase more replacements that are at risk of being infected as well.

The largest area of losses in regards to BVD is the higher rate of abortions and calf mortality from infected pregnant cows. The extent that BVD plays a role in losses has to do with what kind of infection the herd is exposed to. When BVD is introduced into naïve breeding herds, the initial losses due to reproductive failure or clinical disease in calves infected *in utero* may be substantial, but once mature animals gain immunity to BVD the economic losses decrease. This information is useful in examining records; in a herd that is free of BVD, the numbers of abortions and stillbirths should be low (assuming no other reproductive diseases are present). In a subsequent year, if a large increase in these areas is found, it may mean that BVD has been introduced into the herd. Once again this assumption is based on the idea that no other reproductive diseases are present, which in a beef cow herd is never possible. Diseases such as trichomoniosis and

foothill abortion in particular could be other reproductive diseases that could cause a high number of abortions and stillbirths.

In the sector of reproduction, the type of virus plays a large part in the equation of calculating losses. A self-recruiting virulent strain circulating in a herd by persistently infected (PI) animals will show more clinical signs and death loss. An avirulent strain, such as young stock continuously being infected will present less clinical signs. The virulent strains are most likely Type II forms of the virus with the avirulent strains being Type I. Therefore vaccinating against BVD, and decreasing the number of Type II infected animals will undoubtedly lead to more desirable reproductive benchmarks in a herd.

Infection of BVD in a pregnant cow is what causes the reproductive symptoms described. When a gestating cow is infected, the infection will be passed on to the developing fetus as well. Although the anatomical and physiological design of the placenta often acts as a potent defense for the fetus against bacterial and viral agents, the BVD virus is capable of crossing the maternal-fetal barrier. If a cow is infected with the virus during pregnancy, the described effects are highly probable. However, if the cow is infected at a time prior to conception, a slightly better outcome may be expected. This is due to the cow mounting an adequate antibody response to the virus. Once the titers reach appropriate levels, the cow is capable of fighting off the virus to the extent that it may not be passed on to the fetus. The time for a cow to mount an effective antibody response differs with each disease, but in general 4 weeks is usually ample time for an adequate antibody response to be measured. Although the virus is not completely neutralized and the chance of passing the virus on to the calf is still possible, the higher

level of BVD specific antibodies will also be passed on to the calf. Although this is beneficial to the calf, there is still a chance that the actual virus will be passed on as well. More thoughts on this subject are discussed throughout the vaccination protocols in the vaccination portion of the paper.

In regards to the timeline of when the virus is capable of being spread to the fetus, transmission can occur throughout the whole term of pregnancy. But distinct differences, as well as chance of mortality with the calf, are dependent on the specific time of gestation at which fetal infection takes place. Infection during the first trimester of pregnancy will cause stillbirths, mummification, abortion and fetal death. According to (Van Campen, 2010), early gestation infection of fetuses may cause a "storm" of abortions approximately one month prior to parturition. This can be useful information for a producer who keeps accurate, reproductive records year to year. If this so-called "storm" of abortions is witnessed in a herd, BVD may be the likely culprit.

Infection during the second trimester will often lead to a higher risk of birth defects and less abortion. This is more common in beef cattle than dairy breeds. Some of the congenital defects seen may be cerebellar hypoplasia and underdeveloped anatomy of organs and musculo-skeletal system, all of which are devastating to the calf. On the other hand, approximately 1 to 2 percent of calves infected during this time may become tolerant to the infection and become the classically described PI calves that will shed the disease throughout their life (Hansen, 1996). It is these PI calves that have the potential to cause infection to up to 50 percent of other calves prior to weaning (Van Campen, 2010).

Infection of calves during the final trimester of pregnancy does not in all instances cause the fetus any harm. At a stage this late in the pregnancy, the fetus has had adequate amount of passive immunity transfer and has the ability to respond to the virus. Overall losses of calves from conception to parturition may be as high as 50 percent of a total crop calf (Van Campen, 2010). Numbers such as this would prove devastating to any herds, with such a large loss of cattle subsequent income.

Production

This section focuses mostly with dairy herds, as milk production is the factor being examined. Although milk production was always known to decrease in cows infected with BVD, there has been little objective data on the subject until recently. Information from a study performed will be examined for a more accurate assessment of this area.

When examining loss in milk production, most data uses a milk production parameter that also takes into account fat and protein composition in the total volume of milk. This model is similar to the fat corrected milk (FCM) model often used to assess and gauge overall production along milk components. The equation used in a study performed by Heuer et al. (2007) was:

$$\textbf{FPCM (kg/d)} = \exp^{\textbf{intercept + b X lnDIM + c X DIM + d X age}}$$

Where FPCM equals milk volume X percentage fat/ 4.5 X percentage protein/3.2, the variables a, b, c, and d were regression coefficients calculated for each herd, and ln is the natural logarithm of days in milk (DIM). Finally, age was calculated by the days from

date of birth to the test date. The model used 4.5% milk fat and 3.2% milk protein as the standard for components for milk.

Another key factor taken into account that is often left out is the days in milk for each cow at the time of the test, as this will obviously play a large role in the amount of milk given. The herds tested and used by the equation consisted of Holstein, Jersey, and Holstein-Jersey crossbreds. The final findings of this study found that herds with approximately 80% or more of cattle with elevated antibody levels specific to BVD had decreased milk production along with milk solids. The amount of cows with elevated antibody levels within the herd was tested using bulk tank samples. Cows with elevated levels of BVD antibodies were presumed infected with BVD type I or II.

The final conclusion from the study showed that these herds had 0.074 kg less milk solids and a 5.8% decrease in pounds of milk, on a daily basis, than herds with lower BVD prevalence. This decrease in total milk volume along with solids is substantial, especially when applied to a large commercial dairy. Losses such as these compounded over an entire year will add up to a huge financial deficit. Considering the current conditions the dairy industry is facing, a loss in production illustrated above may prove the difference between staying in business or not.

Feeder Cattle

The area of weight gain and carcass quality and its effects due to BVD primarily deals with beef herds but is still very pertinent to dairy cattle. Changes in these traits are especially important with the industry seeing dairy breed steers in a more favorable view in regards to feeding and carcass quality.

In a study performed with a random sample of calves destined for entering a feedyard, 10 of the 56 calves identified as PI calves died before even reaching the feeding facility (Wittum et al., 2001). This figure may be very important for cattle feeders, especially those with contracted cattle that obtain ownership of the cattle before they even reach their yards. Although the data in the study may seem exaggerated and are unlikely, it still shows there is a probability of such high losses.

In another study, Loneragan et al. (2002) showed differing results and a more positive outlook on BVD calves entering the feeding process. The study concluded that the incidence of PI calves entering commercial feedlots was only 0.3%. When looking at this data, one must question where the calves in this study originated. Most likely it was from an operation that implemented procedures against fighting BVD. This shows that, when time and resources are used to combat the disease, there is a positive outcome. One more idea to be considered is, even with a small number of infected cattle entering a feedlot, there is still the opportunity for those few cattle to transmit the disease to cattle in the same pen. The spread of the disease can be exponential as one animal has the potential to spread to many other cattle and so on. Therefore, the number of BVD calves needs to be minimized.

Additionally, bacterial infection of Bovine Respiratory Disease (BRD) has been linked to BVD and vice versa. This connection may be easily understood by taking into account that both diseases will cause the immune system to become weakened, leaving it susceptible to other diseases. Research relating to feeder cattle has shown that BRD is possibly the most detrimental disease found in feedyards. This is based largely on costs of doctoring cattle, but lower average daily gain (ADG) and lower carcass quality are

also factors as well. Therefore, vaccinating for BRD is almost equally important as protecting a herd from BVD when discussing the feeding aspect of cattle.

Economic Losses

In models practiced by European countries, classification of cattle diseases is designated depending on the severity of zoonotic capabilities, animal well-being, compromising food supply, and cost. By using these classifications, BVD is widely recognized as a primary class of diseases. By placing BVD in this class of diseases, it shows the importance of the disease and the possible ramifications it presents (Sandvik, 2004). Within this primary class of diseases, others noted include: bovine spongiform encephalopathy (BSE), tuberculosis, and brucellosis, to name a few. It is easy to see why these diseases rank at the top of importance mostly due to harm they pose to the human population. Although BVD has not been shown to pose any threats to the human population, it still shows the importance of the disease to be classified within this top class of cattle diseases. Probably cost is a large part of the reason why BVD is considered a primary disease. Although this model has been used in Europe and not the U.S., it is still applicable because of the success Europe has had with minimizing the disease and nearly eradicating it in certain countries. Although data is limited and vague, economic losses in U.S. dairy herds are thought to be around $57 million per 1 million calvings (Houe 1999).

Expenses associated with BVD are a major reason for the widespread recognition and concern of the disease. Expenses of the disease are found on both ends; in

preventative measures and also in associated economic losses once the animal is infected. The costs of taking preventative measures can be tracked very accurately. Diagnostic testing of samples (serum, semen, tissue) can be determined with a call to a diagnostic laboratory or the veterinarian performing the tests. The uncertainty of costs lies in the expenses the disease causes on the cattle. A prime example is the PI calf that may not be easily recognized, but will always perform less than average compared to its herdmates.

In determining herds that will suffer more economic losses from BVD, the geographical area is significant. In herds that were located in areas with a high density of cattle, disease is spread more easily, leading to those herds experiencing higher overall economic loss (Sandvik, 2004). This suggests that herds in areas such as the Central Valley in California and specific areas of the Southwest and Midwest regions risk greater economic loss simply due to their location. In less dense areas, expenses have been shown to be more moderate and constant (Sandvik, 2004).

Tying back into the cost-benefit analysis of comparing cost of prevention to expenses caused by the disease, according to Sandvik (2004), testing for the disease will prove to be cost effective, especially with smaller herds. The reason for a smaller herd being more economically efficient in regards to testing pertains mostly to the smaller volume of movement of animals in and out of the herd as well as the feasibility of testing. At first glance it may seem that it is the lesser number of diagnostic tests having to be performed, but in reality the price of running each test per head will pay off regardless of the number of animals being tested. The reasons for more favorable economic effects of testing a smaller herd is the relatively minimal amount of animals being brought into the herd compared to a larger operation.

As noted, with a smaller volume of animals being moved in and out of a smaller herd, it is less likely that the disease will be introduced into the herd. Therefore when testing is performed, for example on a yearly basis, it is safe to say that the number of positive cows will remain fairly similar to the year before if not decreased. In contrast, if a large herd is tested yearly, within one month a large number of cattle may have been moved into the herd, therefore potentially changing the number of positive cattle by a large factor. In effect, the efforts of testing will not gain much; because cattle introduced in the herd may have months to further infect other herdmates before another test is performed.

The limited value of testing conclusion is based on some assumptions that may not apply to all herds. First it is applicable in dairy milking herds or beef mother cow herds. In these operations cows will be kept year round and will likely be kept for multiple years until culled. In a typical beef stocker herd, the carry over from year to year will not be present because of all the cattle being sold within a short time and a new herd being rotated in every year. The second assumption on testing interval made in the previous paragraph was that testing was only performed once a year. In many beef mother cow herds and dairy herds this is the most practical time increment for testing. If performed multiple times a year, larger herds would see the benefits similar to smaller herds because positive animals would not remain in the herd for long of periods of time. Testing a large dairy herd multiple times a year can be performed with relative ease, but in a beef cow operation, once or twice a year is usually all that is possible.

Most of the data dealing with economic losses in cattle have primarily been found with dairy herds, mostly due to more controlled experimental conditions (Duffell et al.,

1986). When examining data retrieved from dairy herds it can be applicable to beef herds as well, but the differences between the two must be recognized. With dairy cattle, the calves have almost no exposure to cows until their first lactation. This does not limit transmission of the disease during pregnancy or from other calves at calf ranches, but it does mean that the calves will be limited in one transmission path. In contrast, beef cattle will be exposed to cows within the herd from birth until weaning. Additionally, dairy herds will calve year round compared to beef cattle calving in a standard fall or spring interval. In the future this is an area that further research could provide a wealth of information for fellow producers.

Pathophysiology and Virology

The diverse and broad nature of the disease is what has led to the umbrella term of BVD being labeled to the group of viruses that cause BVD. Within the categorization of BVD, it is split into two different forms of the virus, Type I and Type II.

Causative Agents and Different Viruses

BVD is a broad term for a wide range of specific viruses which each contribute to the disease. The viruses are classified as a pestivirus of the flaviviridae family. The general classifications of the different viruses are under Type I and Type II with many subgroups existing under each form. Within the Type I and Type II forms, the viruses all have differing levels of complexity along with how they interact with the host animal. This diversity is what leads to some forms of the virus being cytopathic, noncytopathic,

transient, and persistent. Classification under one of these groups is determined by the extent of damage caused by the virus is capable of doing to the affected animal. Through pathological tests and DNA isolation, the genotypes of the viruses are able to be isolated. Although this is very useful information in determining what viruses cause the disease, the practical application of isolating viruses is only to classify a virus under Type I or Type II.

Incubation Period

Determining the incubation period of a virus is useful and important information as part of the complete understanding of how a virus affects the host animal. Many problems exist when determining incubation periods for BVD viruses. First of all the broad spectrum of viruses associated with BVD makes determining incubation period a burden. It should be recognized that each genetically different virus will have different incubation periods within a body. Therefore, as in the case of each BVD animal, the infecting virus is likely to be different or a combination of multiple viruses. Additionally, the immunological status of each animal will affect the incubation period of the virus. In most cases, it will take between 2 and 14 days post inoculation for an animal to show clinical signs or an elevated antibody response against the virus.

Viral Replication

The genetic and antigenic diversity within BVD-causing viruses is wide spread due to the numerous viruses involved with the disease. In a study performed on dairy cattle in Switzerland, 177 BVD strains were isolated and phylogenetically analyzed

(Bachofen, 2010). More specifically, under Types I and II there are at least 13 genetically different subgroups (Pellerin et al., 1994; Falcone et al., 2003; Xu et al., 2006; Jackova et al., 2008). Within these 13 groups the antigenic response of antibody titer mobilization of animals differs by tenfold in crossed neutralization tests (Bachofen et al., 2008). This may mean that each animal is unique in the manner that it recruits different antibodies to neutralize the virus. But most likely it shows that for each different antibody mobilized it corresponds to a different virus. Therefore, this data may suggest that there is a tenfold amount of different viruses classified under BVD.

This diversity of viruses is attributed to antigenic drift, the natural process where a viral RNA mutates, changing the DNA sequence of that virus slightly. Through this new process a genetically different virus is born. With each new virus formed, the risk increases that current vaccines will not have the same efficacy. Therefore, in the future, vaccines may need to be regularly modified in order to have a neutralizing effect on new BVD viruses.

Transmission

Generally speaking, BVD is spread much like any other virus. Virtually any body secretion or excretion has the potential to be carrying the virus. These secretions and excretions will carry the virus for whatever amount of time the virus can live within its specific range of inhabitable conditions. With the mammalian body often being a prime setting for survival of viruses due to factors such as temperature, moisture, and pH, the virus will often not survive long once outside of the body.

The most common modes of transmission are through bodily excretions and secretions from cattle. These may include milk, urine, tears, saliva, semen, fetuses, placentae, reproductive tract discharge, and in some cases feces (Bezek et al., 1995; Brock et al., 1998; Brock et al., 1991; Rae, 1987). Therefore aborted calves along with the associated placenta and discharge may be something that producers should note as potentially hazardous and should handle with caution. In practical terms, the virus is spread most commonly through aerosol and contact with another PI animal.

It is also possible for the virus to spread through fomites such as feeders, troughs and facilities. Although this is a less likely mode of transmission, attention should still be given as a potential area for the disease to spread. In some instances, needles have been shown to spread the virus from a PI animal to other susceptible animals when used intravenously, along with the use of nose tongs when used within three minutes on a PI animal and then to a seronegative animal (Gunn, 1993). Palpation sleeves have also been shown to spread the virus between animals (Fulton, 2002), raising questions about how pregnancy palpation protocols are performed by veterinarians.

Host Animals

Other than cattle carrying the BVD virus, domesticated farm animals have been shown to have the potential of becoming infected with BVD as well. The BVD virus has been found in sheep, pigs and wildlife, although the chance of transmission to or from cattle has not been fully established. Transmission between sheep and cattle has been experimentally proven (Carlsson, 1991), although practical application of this form of transmission has not been shown and is somewhat unlikely due to the fact that cattle and

sheep are rarely in close proximity. The BVD virus has been found in pigs as classical swine fever virus (CSFV), but once again the transmission to cattle is considered doubtful.

Isolation of the virus has been completed in wild ruminant animals such as deer and elk in North America. Initially this was thought to be a possible mode of transmission to and from cattle, and some even thought that the disease may have originated from wildlife populations. Although serological evidence exists that deer can become infected with BVD (Davidson, 1983; Done, 1980; Nielsen, 2000; Grooms, 2002), the existence of PI deer has not been demonstrated.

There is no conclusive evidence that insects are a major vector of the disease, although it has been experimentally shown that the BVD virus was isolated from the non-biting fly *Musca autumnalis*. Therefore, it may be appropriate for further research to be performed in this area.

Persistently Infected Animals

Persistently infected cattle are of the greatest concern for producers when fighting BVD. PI cattle are much more efficient at transmitting the disease due to the higher amount of systemically circulating virus present within the animal. With higher amounts of circulating virus these animals will secrete higher levels of the virus. Additionally PI cattle will secrete the virus in various forms from inoculation of the virus until their death.

The potency of transmission is of major concern as well. It has been shown that horizontal transmission from a PI animal to a seronegative animal can be detected one

hour after direct contact (Fulton et al., 2002). Pathologically, PI cattle are viremic, yet clinically they often show little or no signs of being infected. The classical PI animal is the one that is never shows signs clinically and may seem fine, but in reality is the silent culprit for regenerating the disease. It is for these reasons that PI animals are of greatest concern to producers. Their widespread effects to the herd may be traumatic, making testing, identifying, and culling these animals the most important step producers can take in eradicating BVD from their herd.

Transiently Infected Animals

Transiently infected animals contain lower quantities or less severe forms of the virus in comparison to other BVD infected animals. Therefore these animals are not as efficient at spreading the disease and if spread, as stated, it will be a less severe form of the virus. Additionally, the time taken to spread the virus is considerably longer in time.

The amount of transmission from transiently infected animals may be quantified in herds where all PI animals have been culled. Through seroconversion testing within a herd, an overall figure of how many cattle containing the virus is found. With the possibility of PI animals transmitting the disease being ruled out, all of the transmission must have come from transiently infected animals.

True to their name, transiently infected animals only spread the virus for a short period of time. Once a healthy animal has been exposed to the virus, and a short incubation period has passed, the animal will become viremic and will secrete the virus for 4 to 15 days post-inoculation. It is within this time period that the animal will disseminate the virus to other cattle.

In general, transiently infected animals are more desirable than their PI counterparts. The negative effects caused by these animals will be lower, but one should still not underestimate the importance of ridding the herd of these animals as well. In general, if a herd is to obtain a BVD free status, these animals will eventually need to be culled as well.

Vertical and Horizontal Transmission

Control of BVD targets halting the two modes of transmission that are associated with the disease. These two pathways for the virus are postnatal horizontal infection and gestational vertical infection from a dam passing the virus on to the fetus.

Postnatal horizontal transmission stems from an animal with a transient infection. This animal will shed the disease to herdmates who are in close contact. The problem with this form of transmission is the large volume of animals that the disease can be spread. As we have discussed in high-density areas on a dairy or feedlot, the spread of BVD may be exponential, especially if antibody response within the herd is not strong. Horizontal transmission also leads to vertical transmission as well.

Vertical transmission occurs when a dam that is positive for the virus transmits the disease to the developing fetus. The viremic dam essentially contains a substantial amount of the virus systemically that is capable of infecting the fetus. Calves infected in this manner and also during specific periods of gestation may go on to become PI calves.

Symptoms and Clinical Signs

Clinical signs

Clinical signs of infected cattle cover a wide spectrum from showing no signs to death. The varying clinical signs depend on what form of the virus the animal is carrying along with the extent of the infection. In general a noncytopathic form of the virus will have less detrimental effects than a cytopathic strain of the virus.

Cytopathic strains of BVD will result in more severe reproductive effects including embryonic loss, stillbirths, and congenital defects. Additionally, cytopathic forms of the virus contracted in older cattle will cause these animals to present themselves critically in a clinical setting causing fever, depression, lack of appetite, labored breathing, oral ulcerations, and diarrhea to be observed. In the most severe cases bleeding of internal organs and death have been observed. Supportive care such as fluids and anti-inflammatory drugs may be used, but the likelihood of losing the animal is still relatively high.

Noncytopathic strains of the virus will cause infected cattle to show mild clinical signs if any at all. This form of the virus will create PI calves if they are infected *in utero*, and will cause transiently affected animals if contracted by older animals. This form of the virus is much more mild, giving the animal an opportunity to mount an immune response capable of neutralizing the virus to some extent. Although up to 50% of these animals will appear normal (Larson et al., 2004), some may be noted as having a rough hair coat, unthrifty, mild respiratory disease, and are generally labeled as "chronics".

Secondary Diseases

As with any viral infection in cattle, the initial infection may lead to secondary diseases as well. This is due to the fact that the animal becomes immunocompromised, leaving it vulnerable to other disease. Other than the consequences of reproductive disorders, Bovine Respiratory Disease (BRD) is a major disease that is often coupled with BVD. Bovine Respiratory Disease, much like BVD is an umbrella term for a wide range of bacterial and viral caused respiratory diseases. In a study performed on dairy replacement heifer herds, those that contained high levels of BVD seropositive cattle were at a higher risk of Bovine Respiratory Syncytial Virus (BRSV) (Luzzago et al., 2010). According to Hansen (1996), viruses are the principle pathogenic instigators of BRD, making prevention of BVD key to keeping BRD herd levels at a minimum.

It should be noted that immunosuppression is not the only explanation for BRD being a secondary disease to BVD. Additionally, BVD viruses isolated experimentally have shown to have synergistic effects with other respiratory pathogens (Potgieter et al., 1984; Liu et al. 1999). This explains that one disease may not necessarily be a cause or effect of the other, yet there is a combined, cooperated effort between the virus and bacteria associated with respiratory disease in cattle. Once again, this shows that proper biosecurity, vaccination and treatment of BRD cattle can aid against BVD, and vice versa.

Treatment

Reducing Clinical Effects

It is common for producers to treat BVD animals with antibiotics, thinking it will help the cattle “get over the hump” of whatever they are experiencing. In reality, this

practice will have no direct effect on the infection because a virus is the source of the problem and antibiotics will have no effect on viruses. In animals that are showing clinical effects of BVD, the only true treatment available is supportive. Optimizing the animal's ability to neutralize the virus may consist of reducing fever; countering any nutritional or metabolic disorders and providing basic husbandry practices that one would apply to a diseased animal. Due to many animals showing no clinical signs when afflicted with BVD, oftentimes treatment is not discussed.

Use of antibiotics may be an option in order to prevent secondary diseases such as BRD and in a form may help reduce clinical effects of BVD. An animal with an acute form of BRD will cause the immune system to weaken, allowing a BVD virus to overcome the animal's immune system, causing an acute form of BVD. Within these acute forms of BVD is when clinical side effects are noticed.

Use of antibiotics has been proven to be effective at fighting respiratory infections in cattle. Broad spectrum agents such as Nuflor®, Excenel®, LA-200®, and Micotil®, have the ability to reduce the severity and length of a bacterial infection. In the likely case that an animal is fighting BRD along with BVD, by reducing the extent of the respiratory infection it will reduce the likelihood that the animal shows clinical signs of BVD.

No True Cure

Due to the nature of viral infections, there is no treatment to fully cure an animal of a viral infection. As we have discussed there is a limited amount of treatment that may be performed with BVD animals; the key lies in prevention of disease.

Prevention

The global nature of the disease, along with the ease of transfer between carriers, makes prevention of BVD a formidable challenge. The challenge of eradicating, or even just controlling BVD, can be seen by the statewide and national attempts made by groups of producers to control the disease. Although more recent data does conclude that BVD may be on the decline in certain geographic areas, there is equal data pointing towards the contrary in other areas. Recommendations and practices for prevention of BVD mentioned in this paper will cover multiple subgroups for dairy and beef producers. When the time comes for a producer to implement a prevention program, one must keep in mind that the program must be specifically attuned to the type of operation (cow-calf, stocker, feedlot, dry lot dairy, pastured dairy cattle, dairy calf ranch, etc.). There is no "one size fits all" prevention program. It is crucial that the producer design and continuously adapt a program that specifically fits their operation.

Animal Husbandry

The start of any effective prevention program begins with basic animal husbandry practices. Beef or dairy livestock must first be sustained on a proper nutritional level that fits their energy needs along with maintaining proper body condition. A few points which often lead to a producer overlooking this concept are: price of feed/supplements, inexperience of gauging body condition, and the fact that some simply choose to ignore it. Beginning with the task of supplying an adequate ration to the animal, the price of feedstuffs makes this point challenging from a financial aspect. With the tremendous

increase in price and disproportional increase in return, being able to afford and provide a balanced ration has become a great challenge within the past few years. Although this topic of nutrition exceeds the scope of this paper, one should not overlook the importance of meeting the animal's nutritional needs, especially during immunologically challenging situations.

Tying into the next point of body condition, this idea is a direct result of ensuring an adequate ration is available to the animal. In order to gain useful information on the body condition of a herd, scoring should be done multiple times a year (taking into account seasonal nutritional changes/availability) and should be performed and compared to animals within the same group. Because different groups of cattle will require different body condition scores, the data collected by the producer and veterinarian should be gauged on animals of the same classification; lactating, dry, stocker, youngstock, age, etc. Scoring of the body condition may be done with relative ease, especially with the help of a veterinarian and records should be maintained to compare past results. The importance of not underestimating body condition of the animals is a crucial step in preventing BVD within a herd. Animals under nutritional deficiency may become immunocompromised, hindering the immune response time (Hansen, 1996).

Proper handling of animals is another key preventative measure that should be taken to protect animals from BVD. Expanding on the previous point of maintaining an immunocompotent animal, stress may be one of the greatest factors on the immune system. The shipping/processing time for animals serves as a prime opportunity for cattle to become infected with the BVD virus. Stress along with large numbers of cattle in close proximity allows the disease to be contracted and shed to a large number of cattle in

a short amount of time. Proper animal handling techniques have been shown to decrease stress therefore leading to decreased incidence of disease.

There are some key steps to abide by when attempting to reduce stress by proper handling of livestock. Low-stress handling, transportation and environmental effects are three primary principles that the producer should understand. The idea of low-stress handling emphasizes keeping animals calm and unexcitable. Although the idea of keeping all animals calm during processing is an obvious unrealistic goal, the lowest degree of stress is what should be strived for.

Transporting animals, especially when traveling long distances, is another sector where optimal handling may be practiced. Although there is no way around the fact that cattle may be shipped hundreds of miles at one time, not stocking trucks at 100 percent capacity and taking measures to decrease the time of travel will likely decrease stress. With the common standard of shipping animals as an overall group weight (50,000 Ib), it is not uncommon for multiple producers to commingle cattle from multiple sources in order to maximize the efficiency of transportation expenses. Although this may be unavoidable, these animals will have a greater exposure to pathogens due to the increased number of sources (Thomson, 2006).

Finally, the ambient temperature undoubtedly plays a role in decreasing stress. Processing cattle in all scenarios should take place at times when the temperature is not above 80 degrees Fahrenheit (Hansen, 1996). Although controlling time of processing may not be flexible due to the potential of cooperation of multiple parties involved, efforts should still be taken in the best interest of the cattle. All of the aforementioned handling practices described attempt to aid the animal's defense system to fight off the

abundance of pathogens present in the process. Decreasing the challenges the animal faces by implementing specific protocols will lead to less animals becoming sick and less viral shedding by those that are clinically ill (Thomson, 2006).

Passive Immunity

Adequate quantity and quality of colostrum within the desired 3-hour post-parturition window, is a point that is stressed by bovine veterinarians. The well-known benefits of adequate transfer of immunoglobulins from dam to offspring can be summed up simply by the formation of a competent and responsive immune system. The rewards of immunoglobulin absorption of offspring therefore are linked directly to the protection of clinical diseases including prevention of BVD (Cortese et al., 1998; Ridpath et al., 2003). It was shown that colostral deprived calves experimentally inoculated with a virulent form of Type-II BVD presented severe clinical symptoms and euthanasia was necessary (Cortese et al., 1998). Furthermore, calves receiving colostral-derived passive immunity, and who were challenged with a virulent BVD virus, had capabilities of mounting a protective antibody response against the virus, although antibody titer levels were low (Ridpath et al., 2003). The degree of assistance credited to passive immunity defending against BVD may be disputed, but there is no doubt that some form of defense of BVD is linked to colostral derived passive immunity.

Active Immunity and Vaccination

Although removal of a PI animal is the primary form of halting the shedding of BVD, it has been shown that transmission of the disease will be hindered by an adequate

vaccination program (Larson et al., 2004). *In vitro* studies performed (Larson et. al., 2004) concluded that a wide range of vaccine-induced neutralizing titers were formed in calves with a two-series BVD specific vaccine of either an inactivated or modified live virus form. Further conclusions drawn from the data were that the wide variation of titers allowed for neutralization of varying forms of antigenically different BVD. Various viruses capable of being neutralized included those of American and European dissent, along with the genotypes corresponding to Type I and Type II (Hamers et al., 2000; Hamers et al., 2002). Other important aspects of the study were that the study population was of colostrum-deprived calves. Although the importance of colostrum and passive immunity should not be underestimated, this shows that regardless of degree of passive transfer, vaccines are still effective at stimulating titers in immunoglobulin naive calves. Further studies performed on seronegative cows showed that a single administration of a modified live BVD vaccine stimulated antibodies that were present for up to 18 months and were also capable of neutralizing 12 different strains of BVD (Cortese et al., 1998).

It is apparent that vaccination and passive immunity both offer degrees of protection against BVD but, when coupled together, the combination conferred a potent efficacy against shielding viruses. A study performed showed this from a study group of calves who did receive colostrum and received a single dose of modified live virus form of BVD vaccine. These calves were vaccinated between 10 and 14 days post parturition and were then inoculated with a virulent Type II BVD virus 21 days after vaccination. These calves presented no clinical signs of disease (Cortese et al., 1998). Although these calves may have still become infected with the virus, the fact that no clinical signs were

shown proves that a respectable amount of immune response was capable of fighting off the disease.

Vaccination programs are also targeted at preventing vertical transmission of BVD from the dam to the fetus. In order for this practice to be effective, the vaccinated dam must systemically neutralize the virus (if present), before it crosses the placenta and infects the developing fetus. Earlier studies have shown that most BVD negative cows vaccinated and then experimentally exposed to BVD do provide varying amounts of protection, although this protection was not passed on to 100 percent of the fetuses (Larson et al., 2004). Compilation of research shows that approximately 80% of cattle in the U.S. are given a vaccine with either an inactivated or modified live form of BVD. Although some may see this figure in a favorable view, this number should in reality be very close to 100%.

A final thought to keep in mind in vaccinating against BVD, along with vaccination of any kind, is consistency. In order to bring out the full effectiveness of vaccinating against BVD, the producer must remain consistent. By following a set schedule it will simplify record keeping, and minimize replication and transmission of the virus in the herd. The importance of time of vaccination is one idea talked about when pertaining to pregnant cows along with the whole herd. Likewise, all animals should be vaccinated at the same time of their comparable herdmates. For example, all pregnant cows, stocker cattle, new cattle, should all be vaccinated at the same time ensuring that immunity to the disease is built by the same group of cattle at the same time. This will also protect animals that respond poorly to the vaccination therefore increasing overall

herd-immunity. Additionally it may help in ensuring no cattle slip between the cracks and are missed in the vaccination protocol.

Testing

Testing cattle for BVD is the most important aspect of prevention for the disease. Testing is necessary to obtain a clean herd by identifying positive cattle, and to keep a herd clean by testing incoming animals. Advancements in recent years have increased the accuracy and precision of multiple different testing methods used to identify seropositive animals, therefore decreasing the chance of obtaining false positives. Additionally these tests are now more economically feasible and some do not require samples to be sent in to a laboratory. Producers may now save costs and time by running the samples "in house".

Some key ideas regarding testing must first be understood before the first test actually takes place. Persistently infected animals, in particular, will produce large quantities of BVD particles that may be found in virtually any body tissue at any point past 6 weeks of age. The virus may not always show up in large quantities any time before 6 weeks due to the fact that the calves' immune system is still protected by maternal antibodies. These maternal antibodies have the capability of neutralizing the BVD virus until the colostral immunity wears off around 4 to 6 weeks of age. After this point the virus can be isolated with great consistency. Therefore, testing calves within this time period may result in less sensitive results (Brock et al., 1998; Kelling et al., 1990; Nielsen et al., 2000). Additionally with PI calves, few may develop neutralizing

antibodies that can react with the virus and clear it in serum (Larson et al., 2004). Therefore, white blood samples will be necessary to detect BVD in some PI animals.

Different test methods used by laboratories, veterinarians and producers will be highlighted in the following discussion.

Immunohistochemistry (IHC) is the most practical approach to testing a herd for BVD. Ear notch samples are the most common tissue sample used for this test. This requires little labor in obtaining samples from large numbers of cattle with the use of an instrument such as ear notch pliers and the samples are also suitable for transport. This test is very accurate at identifying PI animals, but cannot provide accurate results for transient animals (Njaa et al., 2000). PI animals contain BVD antigens in all layers of epidermis, making the ear notch sufficient for identifying the virus. In contrast, transient animals contain little or no viral antigens in skin samples. Transient animals will contain the viral antigens in internal organs, but obviously that is an unrealistic source of a sample for IHC.

Ridding a herd of PI animals should be the first step producers take to preventing BVD. Although IHC will miss transient animals, the fact that it allows sensitive and specific identification of PI animals is a step in the right direction (Baszler et al., 1995; Ellis et al., 1995; Njaa et al., 2000). Another attribute of IHC is that cattle tested that had been exposed to a BVD MLV vaccine did not cause false positives (Biuk-Rudan et al., 1998). Contamination of samples from cow to cow is the key concern when performing these tests.

Polymerase Chain Reaction (PCR) tests used to detect BVD have been shown to be more timely compared to virus isolation tests. Additionally PCR has the potential to

detect BVD in it's antigen-antibody complex. Therefore, unlike IHC, this test can be performed on calves under 6 weeks of age, because it makes no difference if colostral antibodies are bound with the antigen (Brock et al., 1998). Polymerase Chain Reaction has the sensitivity capabilities of distinguishing between BVD Type I and II, although the test is not usually used to that specificity. It should not make any difference if a cow is transient or PI; any form of BVD is reason enough for culling.

Another credit of PCR is the sensitivity to detect small very small amounts of the virus within a large sample. This allows the test to be used in pooled blood or milk samples. Through this manner overall herd surveillance may be monitored. A downside to PCR is that due to its sensitivity animals vaccinated within 3 to 10 days may show up as false positives.

Serology is another test that utilizes blood serum as a sample, although semen may be utilized as well. The lack of sensitivity of serology has caused it to be a less desirable form of testing in comparison to IHC and PCR. Although fairly accurate at identifying PI individuals, some situations will cause the test to read cattle as false negatives. Especially in young calves with circulating maternal antibodies in blood serum, these antibodies may cause false negatives if relying on a circulating natural antibodies to determine PI status. This test is not often a choice by producers due to the lack of sensitivity as well as the necessity of using blood as a sample.

Culling

Within any herd attempting to prevent BVD a strict "test and cull" policy must be practiced. Regardless of other factors including worth of animal, market prices, labor

involved, these animals must be removed from the herd. Every day a transient or PI animal is with its herdmates, the potential for the disease to spread will not decrease.

Closed Herd

Once a dairy or beef herd has been tested and is clean of BVD, the next challenge in preventing the disease is maintaining a closed herd. Simply put, any animal being introduced to the herd should be properly quarantined until tested as negative for BVD. At this time it is then safe for the animal to be turned out with other animals. Replacement heifers and bulls raised on a dairy or ranch are obviously exempt from this protocol, because of their origination from the herd.

Maintaining a closed herd is a difficult task for producers to accomplish due to the transition of the beef and dairy industry to fewer and larger farms. This means that a larger number of animals are being moved in and out of farms in a shorter period of time. Additionally rapid growth of dairies in particular has caused an increase in the demand for springer heifers (Van Campen, 2010). In order to meet this demand many dairies rely on calf ranches to fill their need for heifers. Locations such as these are prime areas for a large number of animals to become infected with the virus. Producers should strive to raise all heifers by themselves, but if not possible, all heifers being brought in from outside sources need to be tested before introduction. Similarly, many beef herds will commingle heifers and cows on summer pasture, and if all producers are not protecting against BVD the virus can spread from herd to herd (Sanderson et al., 2000). It is of

particular interest to ensure all breeding cows and heifers are BVD free to make sure these animals do not give birth to PI animals at time of calving.

Conclusion

Planning

As discussed, there is no one size fits all for any operation implementing practices to prevent BVD. The vast differences between dairies, feedlots and ranches dictates that different approaches to the disease will be necessary. Therefore, properly designing a plan of attack against the disease is one of the most important steps producers will take.

First, it must be known if BVD is present in a herd and, if so, to what severity. Before any diagnostic test is performed, an extensive review of records may indicate if BVD is circulating in a herd. Once done, the choice of what diagnostic test to use is the next question. As talked about, IHC seems to be the most commonly used BVD test used by producers although others may be more suitable for other operations. Another important aspect of planning is at what intervals testing will be performed.

Once testing is performed, the producers need to liberate the herd of any BVD positive animals. By repeating testing and culling yearly, along with maintaining a closed herd, a herd will become BVD free. Furthermore, raising and growing one's own heifers and bulls will help maintain a closed herd. The infrastructure of an operation is crucial as well. Ensuring that fences are in good condition, and not keeping breeding

stock in adjacent pastures to a neighbor's herd are two examples that will help maintain a closed herd.

With a clean, closed herd, the only other crucial step to planning is ensuring passive and active immunity is passed on to the cattle. Confirming colostral immunity is passed on to some extent and properly vaccinating cattle will serve as one more line of defense against BVD. By planning and executing these crucial areas, it is likely that BVD may be eradicated from a herd.

Consulting

Fighting against BVD is not necessarily a battle that producers need to take on their own. Maintaining a close relationship with a veterinarian may lead to more specified advice for the producer. Allowing the herd's veterinarian to be an active part in fighting against BVD will be a good insurance policy and will surely help the producer. This may be done through a formal consulting appointment or even through an informal discussion with the veterinarian; either way it will benefit the operation. Finally the veterinarian can be a useful reference for a producer to stay up to date on any new research or ideas on the disease.

Professional organizations such as The Academy of Veterinary Consultants (AVC), American Association of Bovine Practitioners (AABP), American Association of Veterinary Clinicians (AAVC), and numerous breed organizations all provide producers with information on BVD. Resources such as these organizations should be used by producers, especially with the ease of gaining such knowledge through the Internet.

Eradication

As more is understood about the different aspects of BVD, the diversity of the disease makes it a very overwhelming task to overcome. The final goal of eventually eradicating the disease first on a herd level, followed by state and national levels seems unrealistic to many. But many industry and veterinary organizations have taken a bold stance by saying it is possible to eradicate the disease and have outlined benchmarks in order to track the success. In 2001, the AVC drafted and passed a resolution stating their position on BVD. The manuscript states measures to control BVD with the goal of eventual eradication of the disease from North America. The objective of their position statement was: "Therefore, it is the resolve of the Academy of Veterinary Consultants that the beef and dairy industries adopt measures to control and target eventual eradication of BVDV from North America" (Larson et al., 2004). With such lofty aims from a professional organization, it should be thought that this might be a realistic goal. Even if true eradication is never reached, striving for a level such as this will lead to a significant decline of the disease in the U.S.

In the near future, state regulations may be imposed on producers if voluntary programs do not lead to a decline of the disease. Regulations may encompass: herds declaring their BVD status, all animals being sold must be tested, and interstate transport of cattle requiring BVD testing. It is therefore in the interest of the beef and dairy industry to take measures to reduce the disease before mandatory regulations are imposed.

Paradigm Shift

A paradigm shift within the beef and dairy industry is necessary for change to occur. Many producers either are not properly educated on BVD, or else some simply choose to ignore it. With that said, this does not give the industry reason to fully blame producers. Professional and veterinary organizations along with government programs such as state extensions may be more at fault for not conveying the severity of the disease along with the need for eradication.

In regards to a paradigm shift occurring, advancement of the efforts to control and eradicate BVD have not occurred spontaneously and by chance. It has been by a direct and concerted effort. Along with groups and organizations spurring reform, ultimately it comes down to the producer taking responsibility as the agent of change. In the next few years, much will be said about of BVD and the wellbeing of the cattle industry as a whole. One may choose to idly stand by, or make a true difference in the sustainability of our industry and livelihood.

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