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BVD Vaccination, some common sense approaches

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Our knowledge of the bovine virus diarrhea virus is still changing, even though we have known about the virus for many years. One of the things we have learned is that the virus has the ability to mutate readily. The "Veterinary Medicine" BVD review from October 1990 gives a good reference although it is already becoming outdated. The incidence of infected herds appears to be on the rise. This is seen primarily in the dairy herds and purebred beef herds. The BVD viruses appear to have the ability to be tissue specific. Different strains may affect certain organs in the body giving rise to a whole host of syndromes caused by the BVD virus.

Disease Syndromes

The majority of BVD infections are mild or subclinical when they attack the cow or calf. The severity of the infection is determined by the virulence of the strain and the susceptibility of the host. The infection may be completely inapparent as is often seen in adult cattle or may cause a severe disease bordering on the appearance of mucosal disease. The one constant that appears with these infections is an immune suppression. Again the severity and duration of the immune suppression appears to be tied into the strain infecting the animal. In most of these infections, if the animal is unexposed to other disease agents while undergoing the immune suppression, it will recover, however if there is another disease agent present the mortality and morbidity rates can be greatly elevated.

The respiratory syndrome looks very similar to IBR. The predominant signs are upper respiratory tract, primarily the trachea. It can involve the front section of the lungs but usually does not cause much pneumonia by itself.

The newest syndrome is the thrombocytopenic syndrome. It is also called the bleeder or hemorrhagic syndrome. In this syndrome the BVD virus attaches to platelets causing an increased destruction of the thrombocytes. These animals may start with a mild diarrhea or anorexia with a slight fever. The first sign is often bleeding into the conjunctiva. If the owner injects them, the calf will often bleed from the injection site for several hours. On post mortem examination you will find hemorrhaging into the intestinal cavity or internal organs, you may find bleeding in the thoracic cavity or in large muscles. This is caused by a noncytopathic strain and these animals are not persistently infected. It appears to be primarily a disease of the Holstein breed.

In order to understand the remaining syndromes it is necessary to review noncytopathic and cytopathic BVD. There are many different strains of BVD. These can be differentiated using monoclonal antibodies and then grouped into families based on common antigens. All BVD strains are divided into cytopathic (CP) and noncytopathic (NCP) strains. It appears that some of these strains have the ability to mutate from NCP to CP. Cytopathic BVD is rare in the cattle population.

Cytopathic versus Noncytopathic Strains

The CP/NCP differentiation is solely laboratory determined. When a CP strain is grown on a cell culture, the virus kills the cells, whereas a NCP strain does not. The NCP/CP designation does not relate to the virulence of the strain. Some of our most virulent strains *in vivo* at this time are NCP *in vitro*. Clinically you can't tell whether a NCP or CP strain is going through a herd.

Type 1 versus Type 2

Antigenic differences have been found on both the surface (strain variation) and internally on the GP 53 epitope. It is now felt that the pestiviruses can be split into four distinct groups that each share approximately 65% homology with each other. These include type 1 BVD, type 2 BVD, true border disease in sheep, and hog cholera. These internal variations also contain surface variations that appear to be associated with each group. The type 1 versus type 2 designation also does not correlate with virulence. There can be severe death loss with either division depending on the strain. The only group specific disease is the thrombocytopenic form which is seen with only several type strains. The type two strains are not new but the classification is.

Reproductive Syndrome

These differences are still important, however, because of what they may indicate in the herd. The CP and NCP strains react most differently in the non-immune pregnant cow. If a non-immune cow is exposed to a NCP strain while in the first trimester of gestation, early embryonic death, abortion, mummification or persistently-infected calves can result. If exposure occurs during the second trimester, birth defects, primarily involving nervous tissue, or occasionally persistent infection, are found. Infection during the last trimester usually has no effect on the fetus and the calf will be born with antibodies against BVD. Rarely, there is an overwhelming exposure which causes a late abortion.

Persistent Infection

When BVD infection occurs before the immune system has fully developed, the calf learns to recognize the virus as part of itself and never mounts an immune response against that particular strain of BVD virus. Persistently-infected calves can be born normal and constantly shed the virus or they can be born weak and die.

Persistently-infected calves that appear normal can reach adulthood, breed and have persistently-infected calves. They are also a constant source of viral shedding to the rest of herd. The current persistent infection rate in the United States among cattle under one year of age, is estimated at 1½ - 2%. This is similar to the death loss from mucosal disease seen in many feedlots. In some herds, 10-50% of the calves may be carriers. In cow-calf and dairy operations reproductive failure is often the only sign of BVD exposure. Once an animal is persistently infected, nothing can eliminate the virus or stop its shed.

Mucosal Disease

In order for mucosal disease to occur, a specific set of circumstances are required. First, the animal must be persistently infected. Then the animal must be exposed to another BVD virus that is cytopathic. Furthermore, new research indicates that this strain must be closely related to the noncytopathic strain causing the persistent infection to consistently cause mucosal disease. More antigenically distinct cytopathic BVD strains can cause this fatal disease but not as consistently. This exposure may be from additions to the herd or from a persistently infected animal spontaneously reverting to a cytopathic strain. This is the typical textbook BVD with which we are familiar, the explosive diarrhea and ulcers through the digestive tract. Mortality is 95% to 100%.

Chronic Disease

In this form of BVD again persistent infection is a prerequisite. The animal again needs to be exposed to a cytopathic strain. It appears that if the strain is an intermediate in its antigenic relationship to the persistently infecting strain then a three to five month incubation period occurs that allows a recombination of the two strains and the chronic form to appear. These animals may begin with a lameness involving multiple feet or with a mild, non-responsive diarrhea. It often appears like a Johnes case when it begins. The course of the disease is from one to two months and the mortality rate is very high with this complex also.

There is nothing we can currently do to prevent mucosal disease or chronic BVD with vaccination or management except to minimize exposure if possible.

Epidemiology in the Feedlot

Diagnosis

Diagnosis of BVD can be simple or difficult depending on the syndrome under investigation. Mucosal disease and chronic BVD are fairly easy to get viral isolation from the blood if the lab is good. Also submission of ulcerated areas or Peyer's patches will usually yield a positive FA.

The diagnosis of subclinical BVD causing herd

problems can be frustrating. The history will often give some clue. The most common history is that the herd has been experiencing a slow increase in reproductive problems manifested as early embryonic death with a few mummified calves and/or abortions. In some herds the first signs are a higher than expected number of weak and stunted calves or increased calf morbidity and mortality from no one specific etiologic agent.

Serology can be difficult to interpret in these herds. Often by the time a reproductive problem is diagnosed, the exposure has already occurred. The other problem is that if the strain is antigenically different from the reference strain(s) used by the diagnostic laboratory you may get a false negative result.

The level of a single sample titer can be useful to determine if more investigation is needed. Virus isolation can be very accurate if the timing of the sample corresponds to exposure and the laboratory performing the isolation is good.

Confusion exists regarding vaccination programs because of the increasing number of BVD problem-herds being diagnosed. Some of these herds have been on a killed BVD vaccination program, but have still seen a slow increase in reproductive problems over a two to three year period.

There are probably several reasons. One has to do with our ability to better diagnose these infections in the laboratory, particularly the noncytopathic strains. In addition more samples are being submitted for testing. These samples include whole herd testing to find persistently-infected animals. Last, we are seeing an increase in the number of persistently-infected cattle on farms in the United States, probably due to strain variation, the virus's ability to mutate and correspondingly shortened duration of immunity.

Vaccination

Our knowledge about the ability of the different vaccines to protect against BVD infection is increasing rapidly. Recent studies have shown that the duration of immunity afforded by the killed vaccines is dependent on the antigenic similarity between the vaccine strain and the wild type virus to which the cow is exposed. If there are few common proteins, this protection can be as short as four months; if there are many common antigenic sites, it may last a year. Unfortunately, many persistently-infected cows have strains that are antigenically distant (i.e. type 2) to our vaccine strains (i.e. majority are type 1). Thus, these cows are a constant source of infection against which herdmates, if vaccinated with a killed vaccine annually, have little protection. The same holes in protection are found with modified live virus (MLV) vaccines but they do not become apparent until 12+ months after vaccination, closer to the time of annual revaccination and past the time when the virus can cause problems in early pregnancy.

These limitations primarily affect the cow-calf and dairy practitioners; the majority of feedlot veterinarians already use MLV BVD vaccines and these shortcomings are seen if exposure occurs during pregnancy. A total of four studies, several reproductive BVD studies, have been performed. Most have used inactivated BVD vaccines and one has used a combination of an inactivated followed by a modified live BVDV vaccine. Only the last study gave protection at an acceptable level. If you have an open herd or a herd that has had diagnosed BVD problems, you have three options to maximize protection:

1. Increase the frequency of vaccination with the killed vaccines to three times a year. Rotation is probably not necessary with this vaccination schedule.
2. Give a MLV BVD vaccine to the open cow three weeks before breeding or turning in the bull.
3. Institute a virus isolation and cull program along with a vaccination program that includes an MLV BVD to all replacement animals. I start with the young stock and work backwards up the herd to minimize the farmer's cost of testing.

If killed vaccines are only to be given annually, vaccines containing multiple strains will provide broader protection. This protection may still be of insufficient duration to protect against reproductive problems.

Vaccination and Mucosal Disease

Mucosal disease is seen when an animal that is persistently-infected is exposed to another closely related cytopathic strain of BVD. Theoretically, an animal can also have a spontaneous mutation of the noncytopathic BVD strain involved to a cytopathic strain, thereby causing mucosal disease without any subsequent exposure. High stress and immune depression may be involved in this reversion.

One of the major concerns of using MLV vaccines is whether they have the ability to cause mucosal disease. I have never seen this in all the doses I have used in dairy animals. Many of you are also using them without difficulty. Dr. Bolin tried and failed to cause mucosal disease in persistently infected calves by vaccinating with MLV BVD vaccines. It appears that in order for mucosal disease to occur, the CP strain in the MLV vaccine must be closely related to the NCP strain in the persistently-infected animal. With the degree of attenuation of the MLV vaccines today, a second set of circumstances is needed. The second predisposing factor is the background of the animal being vaccinated. If the animal is nutritionally-deficient, persistently-in-

fected and severely stressed, the likelihood of inducing mucosal disease with vaccine may be higher. All of this doesn't mean that the MLV vaccines can't cause mucosal disease, but it does suggest that a specific set of circumstances is required and that disease production, if it occurs, is rare.

You do have options when it comes to BVD vaccination, and you need to realize the limitations of each approach. If a quick and accurate test for BVD is devised, we may be able to start an eradication program. In a small herd, a program of virus isolation, culling and annual vaccination is an attractive option for handling BVD problems. In large herds, the cost of testing may be prohibitive. In such cases, we must assume carriers are present and vaccinate accordingly.

Summary

Bovine viral diarrhea virus infection is being diagnosed with increasing frequency. The number of herds containing persistently-infected carriers is also on the rise. Recent research has shown that killed bovine virus diarrhea vaccines have a duration of immunity as short as four months following vaccination. This may partly account for the increase in infected herds. In order to maximize protection against bovine viral diarrhea, virus killed vaccines must be given three times a year or a modified-live bovine virus diarrhea vaccine can be given annually to non-pregnant cattle.

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