# BVD: WHAT'S THE LATEST

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Bovine viral diarrhea virus (BVDV) is an ubiquitous viral pathogen of cattle that induces disease involving the respiratory, enteric, reproductive, lymphoid, and nervous systems. The diseases commonly associated with BVDV infections are termed acute BVD, mucosal disease, and chronic BVD. In North America, BVDV is a leading cause of economic loss in beef and dairy cattle. Two biotypes of BVDV exist, and these have cytopathic or noncytopathic characteristics in cell culture. The cytopathic virus kills susceptible cell cultures and the noncytopathic virus has little effect on cultured cells. However, there is no correlation between the effects of virus in cell culture and the effects in cattle. Certain noncytopathic BVDV are extremely virulent and kill adult cattle. Conversely, many cytopathic BVDV induce only mild disease in cattle.

Mucosal disease and chronic BVD require simultaneous infection with noncytopathic and cytopathic BVDV. The infection with noncytopathic BVDV occurs in utero, during the first 4 months of gestation, and is persistent. At this early stage of development the fetus does not respond immunologically to BVDV. After birth, cattle with persistent infection remain specifically immunotolerant to certain epitopes on certain viral proteins. These cattle do not normally produce detectable concentrations of neutralizing antibodies against the persistent virus. The infection with cytopathic BVD occurs after birth. The cytopathic virus may come from an external source, such as a vaccine or another bovine, or may arise through mutation of the persistent noncytopathic virus. Once infected with cytopathic virus, the persistently infected bovine may die quickly (mucosal disease) before making viral neutralizing antibodies or may die slowly (chronic BVD) after making viral neutralizing antibodies. Alternatively, the infection with cytopathic virus may not induce disease, but does induce production of viral neutralizing antibodies.

Persistent infection with noncytopathic BVDV is rare, probably occurring in less that 1% of calves. The persistently infected bovine is extremely important to the epidemiology of BVD. These cattle continually shed virus. Thus, the persistently infected bovine efficiently spreads infection to susceptible cattle. Identification and elimination of persistently infected cattle is central to any control program for BVD. Unfortunately, the persistently infected bovine often appears healthy, making visual identification of this condition impossible. Virus isolation from serum, buffy coat cells, or nasal swabs is commonly used for detection of persistent infection. Other procedures for identification of persistent infection are available, but use of these tests has been limited.

Acute BVD is the predominant clinical manifestation of BVDV infection. Usually, this is a mild disease characterized by fever and lymphopenia.

In pregnant cattle, acute BVD may lead to abortion, mummification of the fetus, congenital anomalies, stillbirth, premature birth, weak calves, and persistently infected calves. Through depletive and suppressive effects on leukocytes, acute BVD may enhance the pathogenesis of other infectious agents. Thus, BVDV infections in congregated and stressed cattle may lead to severe respiratory or enteric disease.

Highly virulent noncytopathic BVDV have emerged that induce a fatal disease characterized by thrombocytopenia, diarrhea, hemorrhaging, and death. This disease commonly occurs in veal calf operations but is not restricted to young calves. Adult cattle may develope hemorrhagic BVD and die. Death often occurs after neutralizing antibodies are produced, making post mortem isolation of virus difficult or impossible. The lesions seen at necropsy may resemble those associated with mucosal disease. Hemorrhagic BVD and mucosal disease are differentiated by viral isolation. Both noncytopathic and cytopathic viruses are isolated in mucosal disease, but only noncytopathic virus is isolated from hemorrhagic BVD.

Knowledge of the molecular aspects of BVDV has increased greatly in the last few years. The viral RNA codes for a single large protein that is processed into several smaller proteins. The viral protein, p125, is further processed by cytopathic viruses to p80. The p80 protein serves as a biochemical marker of cytopathic virus. The steps involved in production of p80 are not known, but it appears that an insertion of cellular RNA into the BVDV genome is involved. The p125/80 protein is not a structural component of the virus and does not appear involved in stimulating a protective immune response. The viral protein gp53 contains antigenic sites that bind neutralizing antibodies. Thus, gp53 is important for stimulating a protective immune response in cattle. Among BVDV, there is considerable antigenic variation in gp53.

The antigenic variation in gp53 reflects the high rate of mutation in the viral RNA. Even though BVDV mutate rapidly, exposure to one BVDV stimulates production of neutralizing antibodies that react with all other BVDV. Unfortunately, broadly cross-reactive neutralizing antibodies in serum are temporary. This means that vaccination does not give lifetime protection and frequent vaccination may be necessary to adequately protect a herd. The need for frequent vaccination has been shown by isolation of virus from cattle with BVD several months after vaccination. Monoclonal antibody analysis invariably reveals the virus is antigenically distinct from the vaccine virus.

One approach to the problem of antigenic variation among BVDV is rotation of vaccines used in a herd. Several practitioners have tried this, but the effectiveness of vaccine rotation is unproven. It is possible that either 2 to 3 vaccinations a year with one killed virus vaccine or yearly vaccination with modified live virus vaccine is sufficient to protect against a broad spectrum of BVDV in beef and dairy herds. The feedlot is a more difficult situation. The combinations of multiple stressors and infectious agents found in the feedlot are difficult to reproduce experimentally. Thus, control of BVD in the feedlot is currently more art than science.

Antigenic variation among BVDV affects detection of BVDV and antibodies against BVDV by diagnostic laboratories. Unless optimal conditions are used, certain antigenic variants of BVDV may escape detection when immunostained with standardized hyperimmune serum. Thus, isolated virus may not be detected and negative results reported. Also, the

initial neutralizing antibodies induced by certain antigenic variants of BVDV show little reactivity with standard laboratory viruses. This can make it difficult to interpret viral neutralization tests using paired samples of serum.

Control of BVD will require a better understanding of the antigenic diversity among BVDV. Diagnostic tests and reagents are needed that are not affected by genomic or antigenic variation; and protective immunity must be better defined. Once this is done, immunogens can be assessed on their ability to induce and maintain protective immunity to a broad spectrum of BVDV.