Bovine viral diarrhoea: update on disease and its control

JOE BROWNLI
CBE, BSc, PhD, DSc, LLDBrPhams, DipECVP, FRAS, FRCPath, FRCVSc

RICHARD BOOTH
BSc, BScI, DVM, PhD, MRCVS

In the first of a two-part article look at the syndromes caused by BVDV virus before moving on to review diagnosis of this widely spread disease in UK herds.

ABSTRACT

Bovine viral diarrhoea (BVD) is a widespread infection of cattle throughout the world, although a number of European countries have undertaken national eradication programmes of the BVD virus (BVDV). The virus is classified in the pestivirus genus that also includes classical swine fever virus and border disease virus of sheep.

In recent years, novel viruses have emerged from this genus – some with devastating consequences for livestock health, that is, BVD type 2 viruses and the porcine Bovineonavirus in Australia. The complexity of BVD pathogenesis is focused on the persistently infected (PI) animal; this results from an early fetal infection where the fetus becomes tolerant to the virus and, as a result, remains PI into neonatal and adult life. These animals become the major reservoirs – the ‘super-shedders’ of BVDV.

Understanding this allows veterinarians to design control strategies based on diagnosing and culling these PI animals. Acute infection with BVDV can also cause severe disease, both in young animals through its ability to cause immunosuppression, and in adult animals where it can cause reproduction losses.

Keywords: BVD, persistently infected (PI) animals, musculoskeletal disease, Cumbias, reproductive diseases

The virus

BVDV is a member of the pestivirus genus in the Reoviridae family. All are RNA viruses. It has traditionally contained three members – BVDV, classical swine fever virus (CSFV) and border disease virus of sheep (BDV). In the past decade or more, there has been a greater awareness of other pestiviruses and this has led to a reappraisal of the family relationships (phylogenetic maps). A variant BVDV was identified as the cause of a catastrophic outbreak of acute fatal haemorrhagic disease in the US and Canada in the 1990s. This virus was later classified as BVDV group two, making the original viruses BVDV group one by default. It was then classified the two groups were the highly pathogenic ones and group one viruses were less so. More recent understanding is that virulence does not follow that division. Virus infection and varicella zoster viruses can be found in both groups. However, with the advance of molecular techniques to analyse the RNA genotype of a number of viral isolates from around the globe, a greater complexity of viruses has been revealed. This will be discussed in a later article for Veterinary Times (2014).

The virus exist in two biotypes, a non-cyttopathogenic (NCP) that can persist in cells without causing cell lysis and a cytopathogenic (CP) which does lyse cells. Both biotypes are found in different BVDV groups.

Acute infection

Most BVD viruses are acute, although the acutely infected animal is not the major reservoir of the virus. This is the persistently infected (PI) animal. There has been a tendency for some diagnostics to ignore or disregard the impact of acute infection. There are reasons not to do this.

Highly virulent BVD viruses. Some viruses have mutated to become highly pathogenic and can cause severe disease, if not death, following acute infection. Prominent among the virulent ones, but not exclusively, are the BVDV group two viruses. In the outbreaks in the US and Canada in the 1990s, many thousands of calves died of an acute haemorrhagic disease caused by the group two viruses. In 2013 there was a fatal outbreak of haemorrhagic disease in Germany, with widespread losses of cattle on some 23 dairy cattle and veal farms. The clinical signs were abortions, milk drop and respiratory disease and, in some animals, bloody diarrhoea. In daily cattle, the mortality was up to 20 per cent, whereas in calf units, it could reach 80 per cent. The responsible virus has been typed as a BVDV Type 2c (Doll and Holstet, 2013).
Severe disease has also been recorded in UK cattle, but with BVDV type 1 viruses (Ribdon, Tuckwell, Houghton and Brownlie, 1993).

Reproductive losses. These can range from infertility, abortions and fetal abnormalities to the extra mortality outcome of a persistent infection of a neonate following early viral infections.

Calf diseases. Most calves are born with no experience of infection with BVDV; they are thus "naive" to the virus and have no immunity. Unless they are on farms where there is no BVDV (virgin or BVDV-experienced farms), they are highly likely to become infected in their early years. The virus circulates readily, particularly when there is a Pi animal present. The virus is immunosuppressive and, for a few weeks after infection, will permit the establishment of other pathogens, thereby facilitating cell respiratory and enteric problems. In fact, in those countries and those regions where BVDV has been cleared, there has been a notable improvement in calf health and welfare.

Persistent infection

The Pi animal is the major reservoir of BVDV. Most farm control and eradication programmes require these Pi animals to be identified and culled, and that good biosecurity measures ensure no new Pi are brought on to the farm. Most national BVD eradication programmes depend on this approach.

Our understanding of the creation of Pi animals has not changed over the past few decades. When a BVDV ('naive') dam is infected in early pregnancy, the virus enters the maternal bloodstream, crosses the placenta and infects the fetus. The fetus, at this early stage, is not capable of recognizing or responding to the virus (it is immune-incompetent) and the virus becomes established in fetal tissues. Once it does become immune competent at about 160 to 120 days of gestation, the virus is accepted as a "self antigen" in the process of "central tolerance" to its own tissues. For this reason, Pi animals are always highly infected (so "poor shedder" of the virus) and yet do not make an antibody response to the circulating virus.

Infected during the first trimester (0 to 110 days) of fetal life can result in abortions, congenital damage or the birth of Pi calves.

During the second trimester (111 to 140/150 days), there can be congenital damage and fetal loss.

During the third trimester, the fetus is immune competent and able to mount an active immune response. Pi fetuses, if they don't react, become Pi neonates and some develop into adults and even into breeding stock.

The question remains which happens to the offspring of Pi mothers? Most, if not all, fetuses born to Pi dams likewise become persistently infected. This near 100 per cent vertical transmission from dam to fetus is an important concept for veterinary practitioners to keep in mind when investigating disease outbreaks.

Thus, the question to be asked of all Pi animals is the viral status of their dams. However, the propagation of Pi calves born to Pi dams is reportedly only seven per cent (Gorobatinch et al., 1998), implying the remaining 93 per cent arise as a result of acute infection of the seronegative dam in early pregnancy.

Pi animals are often "stressed" (Figure 1) although many appear clinically normal.

Mucosal disease

Mucosal disease was first reported in 1953 and described as a fatal condition of cattle characterized by severe erosive lesions in the oral and intestinal mucosa (Hamer and Owles, 1953). Over the following 30 years, a series of observations were made about the association between BVDV and mucosal disease. These were finally refined into a hypothesis and proven experimentally.

The hypothesis states an initial transplacental infection of the early fetus with the non-cytopathogenic virus results in the birth of a calf that has a lifelong persistent viraemia. These calves (and only these calves) can then develop mucosal disease as a result of superinfection with a "homologous" cytopathogenic BVDV (Figure 2).

In the field, mucosal disease usually affects animals of six to 18 months of age, although it has been reported in calves of only a few weeks old and even in adult cattle aged five to 10 years.

As there are a number of bovine veterinary-like diseases, the following definition of mucosal disease is suggested: "Mucosal disease is a fatal condition of young cattle that are persistently infected with a non-cytopathogenic BVD virus. It usually occurs between six and 18 months, with characteristic erosive pathology in the oral/intestinal mucosa from which the cytopathogenic BVDV can be isolated. This disease is typically rapid in onset, although chronic obliterating forms can occur."

Reproductive consequences

The bovine responsible for persisting infections following infection in detections is always non-cytopathogenic.
on entering the bull selection programme at about 11 months, he proved to be both antibody-positive and BVDV-positive in semen (but not blood). Later tests established he had a localised, but persistent, infection in his testicular tubules.

From 11 months onwards, Curmus produced infected semen for the following 11 months, at which time (March 1970 months old) he was culled.

So, over the following 15 years, we have seen a small number of either “Curmus” bulls. It does appear a rare outcome of acute infection, but not unique.

For the veterinarian undertaking a thorough examination of a bull, it is essential to consider a semen BVD test, particularly if the bull is sero-positive.

**Diagnosis**

The diagnosis of BVDV-infected animals will be presented in a future and more detailed article. Basically, the diagnostic tests reflect the pathogenesis outlined above. An excellent website for more information on diagnostics can be found on the OIE/WHO website.

**BVDV (detecting infected animals)** requires the demonstration of virus in viral RNA in tissue samples taken from individual animals (blood, milk, semen or ear tag) or pooled samples from a number of animals (bulk milk [BM] or pooled blood samples). Virus can be detected by demonstrating viral protein (by either ELISA or immunofluorescence for viral antigens) or by viral RNA (using PCR).

The only criterion is that it may be important to distinguish between those animals that are either acutely (transiently) or persistently infected. The accepted method is to infect all calves at three to four weeks, by the time, acutely infected animals will have cleared the infection and mounted a specific immune response, whereas PI animals will remain virus positive.

**BVDV antibody.** Antibody indicates animals have been infected. The detection of antibody is most commonly undertaken by the use of ELISA on specific BVDV plates. The real value of antibody testing is it gives a historical view of BVDV infection among that animal or group of animals—this is most valuable in youngstock (usually over nine months) and gives a quick, reliable and economic assessment of the likelihood of the presence of a PI on the farm.

It should also be noted BVDV antibodies can remain high for protracted periods of time (years more than weeks). This needs to be understood when interpreting the presence of antibody in adult animals and most particularly in BM samples. Thus, a single BM sample may have antibody positive, but the source of infection, usually a PI animal, no longer on the farm.

**Summary**

BVDV is a widespread disease in our national herd. It has a complex pathogenesis but, once understood, it prepares the veterinarian for the correct use of diagnostics to control and eradicate the virus from cattle herds.

Valuable websites for reference to BVDV can be found at:
- [www.rcv.ac.uk/bv/index.cfm](http://www.rcv.ac.uk/bv/index.cfm)
- [www.scotland.gov.uk/Topics/farmingandrural/Agriculture/animal-welfare/diseases/diseases/bvd](http://www.scotland.gov.uk/Topics/farmingandrural/Agriculture/animal-welfare/diseases/diseases/bvd)
- [www.ratsolutions.co.uk](http://www.ratsolutions.co.uk)
- [www.dairy.co.uk.uk/technical-information/animal-health-welfare/bovine-security-and-disease/diseases/bdv/bvd/100126PVWY7K](http://www.dairy.co.uk.uk/technical-information/animal-health-welfare/bovine-security-and-disease/diseases/bdv/bvd/100126PVWY7K)

**References and further reading**


Figure 2. The establishment of the persistently infected (PI) cell line following an in utero injection of the fetus with a non-virulent biotype of BVDV, and the consequent development of mucosal disease, after a superinfection with the virulent biotype.