

EDITORIAL

Bovine viral diarrhoea virus: biology, diagnosis and control

Peter Nettleton

BOVINE viral diarrhoea virus (BVDV) is an outstandingly successful virus. It is best known as the cause of a variety of clinical conditions resulting in economic losses in cattle, but understanding its biology has shown that BVDV and other pestiviruses have features unique among viruses.

BVDV causes both transient and persistent infections and can escape the host's immune responses during both events. Transient infection occurs in cattle of all ages. Oronasal infection results in transient viraemia and virus excretion is low before it is eliminated by a standard immune response. The innate interferon response is followed by adaptive cell-mediated and humoral responses so that specific anti-BVDV antibody can be detected within three weeks of infection. Antibody levels continue to rise over the next two months and a solid immunity to that virus is maintained for years.

Peter Nettleton, MBE, BVMS, MSc, PhD, MRCVS, Moredun Foundation, Pentlands Science Park, Bush Loan, Penicuik, Edinburgh, EH26 0PZ, UK
e-mail: peter.nettleton@tiscali.co.uk

However, if infection occurs in a pregnant animal, the virus escapes by crossing the placenta to the fetus where it infects a wide variety of cells without killing them. The tight bovine placentation prevents the dam's immune response from assisting the fetus. Before 120 days' gestation, a fetus lacks a mature adaptive immune response; all viral antigens are accepted as 'self' and are forever seemingly ignored by the fetus' or calf's cell-mediated and humoral adaptive responses. The fetus is immunotolerant to those viral antigens and will not respond to them throughout the rest of its life. The virus has simply escaped the host's adaptive immune response resulting in an animal that is persistently infected.

The virus also has to circumvent the host's innate immune response, which is fully functional from the embryo's early development, from the first day of fetal infection throughout the host's life. BVDV is able to combat interferons, which are key components of the innate antiviral defence system. The viral RNA contains two genes coding for proteins that are unique to pestiviruses: the N-terminal autoprotease (Npro), and a structural envelope glycoprotein

with RNase activity (Erms). The first reduces intracellular interferon production and the second degrades extracellular BVDV RNA, thereby preventing its recognition by receptors that signal the presence of an RNA virus to the host. (Peterhans and Schweizer 2010).

The calf is born persistently infected with BVDV and once passive colostral anti-BVDV antibodies have decayed, it will continuously excrete millions of infectious virions every day of its life. Approximately 1 per cent of one-year-old cattle are persistently infected. Close contact with a persistently infected animal results in naive cattle becoming transiently infected and seroconverting. The success of the virus spread by persistently infected animals can be judged by antibody prevalence rates greater or equal to 60 per cent in adult cattle within infected herds.

Knowledge of the epidemiology of the virus aids diagnosis and control. In live animals, it is usually more cost-effective to look for BVDV antibodies in blood or milk from a group of cattle as an indication of the presence of a persistently infected animal than to hunt the rarer virus-positive, antibody-negative persistently infected animal.

Dairy farmers can readily determine and monitor the BVDV status of their herds by bulk milk antibody testing. A paper by Booth and others (2013), summarised on p 449 of this issue of *Veterinary Record*, has made a practical contribution to understanding the BVDV status of dairy herds by using bulk milk antibody testing, since vaccination use and presence of BVDV infection were also monitored.

Regular bulk milk antibody titres were recorded over three to four years from 14 dairy herds, a subset of 30 dairy herds that were members of a pilot BVDV eradication scheme which had been established in Somerset, England (Booth and Brownlie 2012). The 14 herds, all with pre-existing mid- to high-positive bulk milk antibody levels, were grouped into three categories: category 1, vaccinating and no persistently infected animals present (n=6); category 2, not vaccinating and no persistently infected animals present (n=2); and category 3, vaccinating and persistently infected animals present (n=6). Category 1 herds showed a slow progressive rise from mid- to high-positive bulk milk antibody levels with transient increases following vaccination. Category 2 herds showed a progressive decrease from mid-positive, with one herd taking three-and-a-half years to become negative. Category 3 herds began



Picture: Moredun Research Institute

Farmers who have eradicated bovine viral diarrhoea from their farms have reported improvements in calf health, including a lower number of calf deaths, better resistance to disease and fewer antibiotic treatments (Scottish Government 2013)

the study with high positive bulk milk antibody levels that remained so, but, again, transient increases following vaccination were detected. There were fluctuations in monthly antibody titres in most herds, emphasising the need for regular bulk milk antibody testing. Encouragingly, the eight dairy herds in categories 1 and 2 stayed free of BVDV throughout the study, thus confirming that, with good biosecurity, BVDV-free herds can be established and maintained in a cattle-dense region.

The authors include interesting observations on farmer compliance and recognise that only one antibody detection ELISA and largely one vaccine were used; other antibody detection ELISAs are available and their use is discussed. Their major conclusion was that the interpretation of positive BVD antibody levels in bulk milk is not straightforward without some follow-up testing of youngstock.

Dairy farmers are under relentless time and cost pressures and deserve every assistance to improve the health and welfare of their herd using well-validated strategies based on biosecurity, removal of persistently infected animals and surveillance methods (Lindberg and others 2006). Booth and colleagues are to be congratulated on their detailed documentation of real farm scenarios, which should inform dairy farmers and vets on ways to proceed.

The impetus to eradicate BVDV in Europe is gathering pace. The Nordic countries are free and Austria, Switzerland and Germany have advanced programmes;

the Shetland Isles are free, Scotland and Ireland have compulsory programmes in place and Northern Ireland has started a voluntary scheme; England and Wales are consulting. It is essential that all stakeholders – farmers, vets, advisers, scientists, and those responsible for markets, abattoirs and the food chain – are kept informed and work together (Voas 2012).

As schemes proceed, veterinary vigilance is paramount. Problems will

arise because BVDV is genetically diverse and its global status is always changing (Ridpath 2010). Continuous surveillance of BVDV isolates and disease associations will be vital to ensure vaccines are working and that diagnostic tests are relevant. Fortunately, new fast and cost-effective technologies have recently been developed to monitor BVDV diversity (Bachofen and others 2013), but these are only as good as the samples from the farm.

References

- BACHOFEN, C., WILLOUGHBY, K., ZADOCKS, R., BURR, P., MELLOR, D. & RUSSELL, G. C. (2013) Direct RT-PCR from serum enables fast and cost-effective phylogenetic analysis of bovine viral diarrhoea virus. *Journal of Virological Methods* **190**, 1-3
- BOOTH, R. E. & BROWNIE, J. (2012) Establishing a pilot bovine viral diarrhoea virus eradication scheme in Somerset. *Veterinary Record* doi:10.1136/vr.100191
- BOOTH, R. E., CRANWELL, M. P. & BROWNIE, J. (2013) Monitoring the bulk milk antibody response to BVD: the effects of vaccination and herd infection status. *Veterinary Record* doi:10.1136/vr.101195
- LINDBERG, A., BROWNIE, J., GUNN, G. J., HOUE, H., MOENNIG, V., SAATKAMP, H. W., SANDVIK, J. & VALLE, P. S. (2006) The control of bovine viral diarrhoea virus in Europe: today and in the future. *Revue Scientifique et Technique* **25**, 961-979
- PETERHANS, E. & SCHWEIZER, M. (2010) Pestiviruses: How to outmanoeuvre your hosts. *Veterinary Microbiology* **142**, 18-25
- RIDPATH, J. (2010) Bovine viral diarrhoea virus: global status. *Veterinary Clinics of North America: Food Animal Practice* **26**, 105-121
- SCOTTISH GOVERNMENT (2013) BVD eradication case studies 2013. www.scotland.gov.uk/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/bvd-case-studies-2013
- VOAS, S. (2012) Working together to eradicate BVD in Scotland. *Veterinary Record* **170**, 278-279

doi: 10.1136/vr.f2526

Veterinary Record publication times

Acceptance rate	33 per cent
Time from submission to first decision (median)	23 days
Time from submission to acceptance (median)	35 days
Time from acceptance to online publication	27 days
Time from acceptance to print publication (research summary)	62 days