BVD — why vaccination alone is not the complete answer to eradication

This article is primarily about controlling and eradicating bovine virus diarrhoea virus (BVDV). For some, it might appear to be just a repetitive article about bovine virus diarrhoea (BVD) but it is hoped it is more than that. It would be good to explore in greater detail the value of vaccination in the process of controlling an infectious disease.

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By its very nature, an infectious disease is infectious and will transmit from host to host. The process of transmission will influence the rate and range of that movement from infectious to non-infectious naïve hosts. Thus aerosol spread has the potential to move rapidly and widely; this was apparent with foot-and-mouth disease virus (FMDV) in 2001. If the infection is spread by mosquitos/midges, then it will be determined by the insect breeding season and possibly by wind. This was seen with Bluetongue virus (2007/2008) and more recently with Schmallenberg disease virus (SBV) in 2012. There is also the potential for canine distemper to re-emerge and recently a new canine coronavirus has been recognised (Erles et al, 2003). These are interesting examples as there is a different control strategy for each infection and not all include a vaccine element.

In the UK, foot and mouth disease (FMD) is controlled (initially at least) by a culling programme orchestrated by the government services. Admittedly in other countries with endemic FMD, a vaccine programme is undertaken. With the incursion of Bluetongue in 2007/2008, a specific BTV8 vaccine was developed and made available to farmers. Again with Schmallenberg disease virus, a vaccine has been developed and registered for use in the UK. Canine distemper has all but disappeared from most parts of the UK following the widespread use of the multi-component puppy vaccines. All new or re-emerging diseases do, however, need to await the development and registration of safe and efficacious vaccines (a story in itself).

Why vaccines are critical in disease control

It is said that only clean water has proven to be more effective in the control of infectious disease than vaccines. Vaccines have transformed the ability to control and even eliminate many of the epidemic diseases that have punished both human and animal populations over the years, e.g. smallpox, rinderpest and polio. It is curious that the anti-vaccine lobby is so vociferous when the successes of vaccines are so evident. It is perhaps, to some degree, how vaccines are used; vaccines need to be correctly stored, transported and used as indicated by their data sheets. Few vaccines give 100% protection, if any, but when used correctly they can be highly efficacious. The issues about giving them correctly are not trivial and will be revisited later in this article.

There are further reasons for the continuing, if not growing importance of vaccination programmes. In viral, bacterial and parasitic diseases, their increase in drug resistance is alarming and the rate of development of new drugs is woeful. Vaccines offer a lifeline and provide a sustainable therapy. However, it has not been possible to construct protective vaccines against all pathogens in all species; some are notoriously difficult such as Hepatitis C, HIV and malaria and, dare it be mentioned, tuberculosis.

So what about bovine virus diarrhoea (BVD) and BVD virus (BVDV) vaccines?

BVD disease and control

Much has been written about BVD, the disease and its control (Brownlie and Booth, 2014). In essence, it is a widespread and important viral disease of cattle, affecting both reproductive performance and calf health. It is no longer correct to say it is global as a number of European countries have, or are, undertaking national eradication programmes (Scandinavian countries, Switzerland, Austria, Germany, Scotland and Ireland) while others have regional programmes. In England, it is anticipated!

The central part of the pathogenesis is that BVDV can infect the naïve dam in early pregnancy and, following a brief viraemia, the virus can reach and cross the placenta, that as a consequence, infects the developing fetus. The term 'naïve dam', refers to a dam without immunity to the virus, i.e. never naturally

infected or vaccinated. The early fetus (up to about 110–120 days of gestation) is not sufficiently developed immunologically to recognise the virus as a 'foreign invader' and tolerates it. The result of this is that when the immune system is sufficiently competent, it must disarm any immune recognition of its own tissues (to avoid auto-immunity) and in that process disarms (tolerates) any immune recognition of the virus. The virus becomes a 'self antigen'. The result of this is that the virus can persist for the life of the fetus and, in fact, for the lifetime of the animal, even into old age. As it remains forever tolerant, it does not produce BVD antibodies to this persisting virus. This is the animal that is considered persistently infected (PI). They are the main reservoir for all livestock infections.

So there are two choices about controlling onward infections with BVDV: ensure that all PI animals are recognised and removed (preferably culled) from other livestock (Lanyon et al, 2014); or ensure all dams are protected during early pregnancy from BVD infection, i.e. by good biosecurity and/or vaccination? Or possibly both!

How successful does the vaccine need to be?

It is generally assumed that any vaccine that gives greater than 80% protection is valuable. At this level, a marked reduction, or even absence, of clinical signs would be expected. If we are talking about vaccines used in calves against RSV, PI3 or even BVD they can reduce coughing or enteritis and thereby significantly reduce the onward transmission of infection and thus minimise the scale of the outbreak. They also may reduce the infectious dose during transmission and allow a naïve animal a better chance to mount an effective immune response. It is often found that there is a dose-dependent effect with epidemic infectious diseases. As an epidemic develops, more animals are excreting more virus (or other pathogen) and so the infectious dose becomes overwhelming for any new infection. To make matters worse, some viruses can mutate during the early stages of an epidemic to become more virulent — thus the challenge is both higher and more dangerous. If BVD is used as an example, it is also found that more virulent strains grow to higher levels in infected animals and transmit more readily.

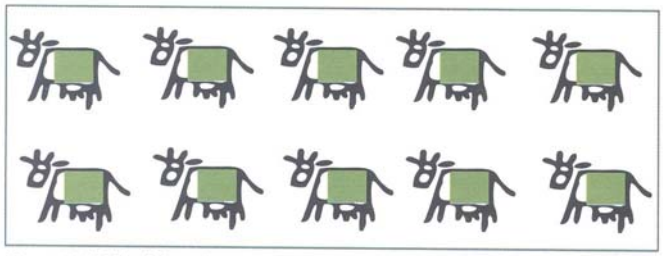

Figure 1. 100% of dams have 80% protection against BVDV. This is inadequate to give complete protection against fetal infection in 100% of dams.

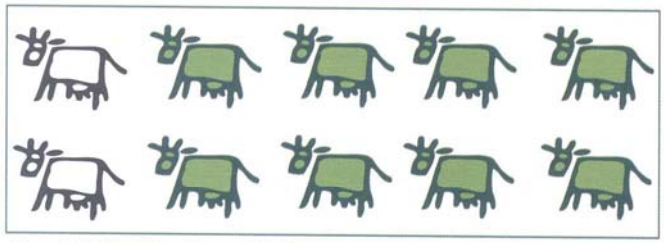

Figure 2. 80% of dams have 100% protection against BVDV. This is adequate to give complete protection against fetal infection in 80% of dams.

Why are BVD vaccines demanding to make and to give?

Returning to BVD vaccines. Why are they so demanding to make and to give? If talking about just the single BVD component of a multi-component calf respiratory vaccine, then 80% protection or above might be adequate to give protection. However, when considering fetal protection, the situation is quite different. The aim here is to prevent any viral particle gaining access to the placenta as, once it has infected the maternal placenta, it can 'grow' across the interface and infect the fetus. The bovine placenta is sufficiently thick with five layers and total integrity (no leakage) that no maternal immunity can cross to the fetus to help it in its early immune-incompetant period. Thus it cannot influence the process of the fetal PI described above. So the vaccine must give 100% protection not 80%, not even 99% (*Figures 1 and 2*)!

So the demands to make efficacious BVD vaccines are high. There are well understood concerns about live attenuated BVD vaccines and so, at present, only killed BVD vaccines are available in the UK. They are safe but the demands to provide strong and continuing protection requires close attention to handling the vaccine correctly (not half-used vaccines left on dairy shelves or, worse still, in the back of hot cars). More importantly they should be used to the data sheets and, where there is a request for two priming doses before heifers enter the breeding programme, that is a critical requirement. A number of surveys examining BVD vaccination on farms found that less than 30% of BVD vaccines are given correctly. Reducing the efficacy of a BVDV vaccine by just a few percent will render it useless.

However, BVD vaccines used correctly are fine 'tools in the tool box'. Vaccines are, as mentioned at the start of this article, marvelous developments and BVD vaccines are no less!

When do you use them?

This is the rub; when to use them? Assuming that they will be used correctly from now on (not perhaps a wise assumption), if they give good protection in the majority of animals, why not just vaccinate and wait for elimination of the virus from the herd. This could be done and it may be successful but it might be necessary to wait a while, if not a very long time. The reasons that no vaccine is 100% across all recipients, are that they must be given correctly (as discussed above) and that, with the BVD transmission from a PI animal, the challenge is extremely high and continuous. Finally, remember that only 1–10 viral particles are needed in the placenta to enter the fetus. Far better to try to reduce this risk from PI animals by eliminating them first – this will be discussed.

KEY POINTS

- Controlling infectious diseases by vaccination has been, and will continue to be, crucial.
- Vaccines need to be given correctly; a high proportion are not.
- Bovine virus diarrhoea (BVD) vaccines are particularly demanding as they need to totally prevent viraemia.
- BVD vaccines used correctly are valuable.
- To eradicate BVD, vaccines need to be given within a strategic approach; remove persistently infected (PI) animals, maintain effective biosecurity and appropriate vaccination.
- BVD vaccines used on their own are unlikely to eradicate BVD.

Possibly the biggest risk from the use of BVD vaccines is not about the quality of the vaccine but about the thinking that all vaccines are 100% and that nothing else needs to be done. Polio vaccines, measles vaccines, distemper vaccines are all wonderfully protective and have made a huge impact on the control of these dangerous diseases. So it is easy to understand the mentality that says 'vaccines alone' should do the trick. Unfortunately with BVD it is not true.

Why is biosecurity so difficult to 'sell'?

In fact, BVD vaccines may help with control on a farm but, when used incorrectly, do not help with eradicating the disease within a community. With BVD, vaccines need to be used within a strategy that reduces the risk of infection by both diagnosing the PI animal and culling it from the herd (and not releasing it back on to the market where it spreads the infection to the unfortunate purchaser).

Furthermore, it is crucial to understand, believe in, and undertake sensible and informed biosecurity. It is all too easy to reintroduce infection into the herd through infected animals, dams carrying infected fetuses or infected materials, syringes or fomites. It is difficult to understand why biosecurity has such a stigma; it is so much in the interest of the owner to undertake it. Imagine having a neighbour with drug-resistant tuberculosis or influenza, most people would be very cautious and undertake strict biosecurity. With a herd of prize animals, I would do the same — even a herd of not prize animals! Two good reviews well worth reading have been recently published (Orpin and Sibley, 2014; Sibley, 2014).

The way ahead — what works?

There is little doubt that it is possible to eradicate BVD without the use of vaccines — the Scandinavians have shown the way. They had a complete national programme which, although voluntary to start with, was subsequently an enforced programme with legal power. However, where there is a voluntary programme over a longer period, and with possibly less farmer take-up, there is a real need to provide both a way to reduce the virus-load on infected herds and also to protect those herds that have gone BVDV free. Both the Scottish scheme (Voas, 2012) and the Irish scheme (Graham et al, 2014) are making good progress, neither have banned the use of BVD vaccines. There is a place for the correct use of vaccines but not a place for the total reliance of vaccines without an informed strategy to eliminate the major source of virus — the PI animal.

Conclusion

In this article, the value of the importance of using BVD vaccines correctly has been explained. They can have a role in an eradication scheme but, for such a scheme to succeed, they must be used within a strategy that includes identifying and removing the major reservoir of the virus (the PI animal), maintaining a risk-based biosecurity and giving the vaccines correctly. LS

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