Practical vaccination strategies for beef cattle

M. Daniel Givens, DVM, PhD, DACT, DACVM (Virology sub-specialty)

Virginia-Maryland College of Veterinary Medicine
Blacksburg, VA 24061

Abstract

The identification and adherence to underlying principles for the development of practical vaccination protocols for beef cattle operations can lead to clear, prudent and justified recommendations to producers. Consideration of results from clinical trials should clearly inform decision-making in the formation of these recommendations. In some situations, the determination of how to prioritize and apply underlying principles will require a thoughtful, iterative process between the veterinarian and the producer. The result of the process should lead to the development of an optimal, tailored protocol and a close professional relationship between the veterinarian and the producer.

Key words: cattle, beef, vaccine, IBR, BVDV

Underlying principles for practical vaccination

The consideration of underlying principles for practical vaccination strategies should guide decision-making regarding how best to stimulate needed immunity. Needed immunity is considered the immunity to pathogens that are likely to be encountered and likely to cause significant disease during the life of the animal. Protective immunity is considered an immune response that will prevent disease when the animal is exposed to a pathogen under field conditions. Underlying principles state foundational facts that should be considered to develop the best practical application of vaccines in beef operations. In the case of each herd or management unit, prudent determination of how to prioritize and apply underlying principles will best determine the optimal, practical vaccination protocol for particular beef cattle operations.

Vaccines are prudent and recommended though no vaccine is 100% safe and effective

The goal of vaccination is immunization. Vaccines can be generally categorized as modified live vaccines (MLV), killed (inactivated) vaccines, or genetically engineered vaccines. Modified live vaccines are designed to induce a mild immunizing infection. Viral strains are often attenuated through serial passages in cell cultures to produce the strain of virus used in an MLV. Regrettably and very rarely, the process of cultivating virus for production of an MLV can result in the presence of extraneous live viruses in the vaccine.[1] If the vaccinate is immunocompromised, vaccination with an MLV may cause a problematic infection that results in disease or abortion. Though relatively rare, vaccinated animals may shed the modified live pathogen[2] to contacted animals who may develop disease or abort. This has been demonstrated not to occur with some modified live vaccines.[3] Modified live vaccines commonly provide greater efficacy at the expense of potentially causing illness. Modified live vaccines do exhibit lowered stability as the agent in the vaccine must be maintained in a viable manner. A single dose of MLV can often be sufficient to produce protective immunity.

Killed or inactivated vaccines may maximize safety at the expense of efficacy. In some situations, the safety and stability of killed vaccines may compensate for their immunologic inferiority. At times, killed vaccines are a prudent recommendation for pregnant heifers and cows and for stressed calves. Inactivation of vaccine components also eliminates concerns about replication of contaminants in the vaccine. Killed vaccines contain adjuvants that are effective in priming immune responses but may cause more significant tissue reactions. While oil-in-water or water-in-oil emulsions can be very effective adjuvants, they may stimulate inflammatory reactions and significant tissue reations.[4] As a general rule, two inoculations of a killed vaccine are often necessary to stimulate protective immunity. Thus, the stimulation of an effective immune response is slower with a killed vaccine that with an MLV vaccine. For a killed vaccine, the delivery of a full dose containing the complete antigenic mass is important to stimulate protective immunity. Compliance with appropriately timed multiple dose administration of a killed vaccine may be practically challenging.

Genetically engineered vaccines can be categorized as subunit vaccines, gene-deleted vaccines or vectored vaccines. These types of vaccines are rare in day-to-day vaccination of cattle in the United States and yet, are considered to hold some promise for future vaccine development.[5] These vaccines can be subcategorized as subunit vaccines, gene-deleted vaccines (also known as marker vaccines) and vectored vaccines. Subunit vaccines consist of purified antigenic viral proteins that are mass produced by molecular cloning mechanisms (high copy number plasmids). These viral proteins may be inserted into immune stimulating complexes (ISCOMs) to increase antigenicity. Like killed vaccines, subunit vaccines are considered safe though the entire antigenic mass must be provided in the vaccine dose.

Gene-deleted vaccines are produced by using methods to cut and remove specific genes from vaccine viruses. Thus, this type of a vaccine can allow differentiation of a vaccinated animal from an animal that was infected with a field strain of the pathogen. Therefore, gene-deleted vaccines can be ideal for use in coordination with a regional or national eradication program. These immunizing strains are unlikely to revert to virulence in absence of co-infection of the vaccinate with a field strain of virus. Thus, they are considered safer than classically attenuated MLV. Yet, gene-deleted vaccines can rarely be contaminated with extraneous viruses that may cause significant disease.[6] Vectored vaccines are produced by inserting genes that code for antigenic proteins from one virus (the vaccine agent) into a carrier agent (vector). The vector is selected to infect and replicate in animals without causing disease. Vaccinia virus-vectored oral rabies vaccine for administration to wildlife is an example of a vectored vaccine.

Basis for selection of vaccination protocols

Vaccination protocols should be selected based on (a) risk of disease introduction, (b) vaccine protocol efficacy, (c) vaccine protocol safety, (d) cost of vaccine and vaccine administration, (e) convenience, and (f) the production benefit received by the producer. If the risk of disease introduction – which differs in some cases from introduction or encountering a pathogen – is negligible, then vaccination for the particular pathogen may be a poor decision. If the resulting reliability is high for protection from a likely and significant disease, then a particular highly efficacious vaccine protocol should be considered very favorably. However, the risk of disease and resulting efficacy of the protocol must be weighed against the safety of the vaccine protocol in accordance with the principle of *primum non nocere*. The benefits of effective vaccination (if and only if exposure to the specific pathogen of concern occurs) may include increased pregnancies, prevention of fetal infections, increased live births, an increase in the number of calves weaned, and an increased overall weight of calves weaned. The natural costs and consequences of cattle handling and vaccine administration commonly include additional stress of cattle due to handling and vaccination, a transient loss in production (such as weight gain), and injuries to some animals due to handling.

As the benefit of immunization is only realized if the risk of disease introduction is significant, quantifying the risk of pathogen introduction and resulting disease may be helpful in determining vaccine protocols. For bovine viral diarrhea virus (BVDV), the risk of introduction of a persistently infected animal may be calculated as:

$$Risk\ of\ introduction = 1 - NPI^{n}$$

Where NPI = the probability of a non-persistently infected animal and n = the number of animals purchased. Thus, as an example, if a geographic region has a prevalence of persistently infected animals of 0.4% (4 PIs per 1,000 head; which is the average resulting from several large prevalence studies) and a producer is purchasing 100 untested heifers to add to an existing unvaccinated herd, then the risk of introduction = $1 - (99.6\%)^{100} = 33\%$.[7] Understanding the likelihood of bovine herpes virus-1 (BHV-1; infectious bovine rhinotracheitis; IBR) causing an abortion or an abortion storm is more challenging. In 1973, IBR was diagnosed as a causative agent in 24% of bovine abortion cases submitted to diagnostic laboratories in one study. That rate of detection of IBR in cases of bovine abortion submitted to diagnostic laboratories dropped to 5% or less in similar surveys conducted in 1992, 2004, 2013 and 2016. That substantive decrease is associated with the unique history of the use of MLVs containing BHV-1 in the United States. Modified live-virus vaccines containing BHV-1 were introduced in the U.S. in 1956. In spite of mounting evidence from the field, it was not until 1964 that manufacturers conceded that the available MLV vaccine was not consistently safe for use in pregnant cattle between the third and eight-month of gestation.[8]

The convenience of vaccination protocols is particularly important if the protocol is to be consistently implemented and become a routine part of the cow-calf operation. The best time to vaccinate cattle may not be the most convenient time. The most convenient time to vaccinate cattle may not be the best time. Between these two extremes, determining the optimal time to vaccinate cattle depends on the science of effective immunization, the impact of external determinants, the efficacy of communication, and the trust that is to be developed and maintained between a veterinarian and their client.

Reasons that prudent vaccination strategies are disregarded include: (a) the necessity of immediately, and sometimes unexpectedly, introducing reproductively sound animals to the herd, (b) the proposer of vaccination protocols was more intolerant of risk than the person paying the bill for the vaccination protocol, (c) the lack of available resources including labor, facilities, and/or a specific vaccine at the appropriate time, and (d) the lack of clear, prudent, and justified recommendations. As indicated previously, immunity is not immediately conferred upon the withdrawal of the injection needle from the animal. This fact may be important to communicate to the producer to ensure realistic expectations, particularly when a killed vaccine that may require multiple doses is being used.

Finally, a prudent vaccination protocol will not outperform or ever fully replace sound management that involves appropriate biocontainment and biosecurity. A valuable cautionary tale can be gleaned from an experience where a producer-backgrounder was band-castrating 600-pound bull calves at the time of purchase from a sale barn. Concurrently, the producer was vaccinating the calves with a commercial product containing *Clostridium perfringens* Type C&D and tetanus toxoid. The producer maintained this practice for three or four years without incident, then experienced the death of seven calves at seven to 12 days after vaccination and banding. Based on clinical signs and post-mortem exams, the attending veterinarian diagnosed tetanus as the cause of death. While the producer raised concern regarding the efficacy of the product in the year of the seven deaths, the reason there was not loss of calves in the preceding years was not because the calves were protected at 7 to 12 days after banding and first vaccination, but in all probability because there was no natural tetanus challenge until the year when calves were lost. It is a fact that calves will not have adequate, protective immunity at 7 to 10 days after their initial vaccination with a product containing *Clostridium perfringens* Type C&D and tetanus toxoid. This production challenge can be corrected by altering the timing of vaccination in relationship to the banding or using a tetanus antitoxin instead of toxoid. Tetanus antitoxin is more expensive and provides more rapid – though transient – protection from tetanus.

Protection against disease losses due to IBR and BVDV

A meta-analysis of randomized, controlled, clinical vaccine trials with experimental challenge to assess prevention of abortion demonstrated that both killed and MLV vaccines containing BHV-1 will significantly prevent abortions.[9] A meta-analysis of vaccine trials to assess prevention of fetal infection with BVDV demonstrates that MLV vaccines containing BVDV are often more effective than killed vaccines in preventing fetal infection.[10] For evidence from a specific vaccine trial, administration of two doses of a commercial vaccine containing killed BVDV strains prior to breeding resulted in 27% fetal infection when pregnant animals were exposed to persistently infected cattle from 52 to 150 days of gestation.[11] The greatest risk for fetal infection with BVDV occurs after the introduction of new cattle into a herd. This risk increases exponentially based on the number of new cattle that are introduced.

Modified live vaccines containing BHV-1 present significant potential safety risks when heifers or cows are vaccinated shortly prior to breeding or when pregnant heifers or cows that were not previously vaccinated are administered vaccine. Vaccination or re-vaccination with an MLV containing BHV-1 is

recommended at no less than 30 days before breeding. Clearly, re-vaccination presents a much lower potential risk than the initial administration of vaccine during this time-frame. The adverse event rate in this situation has been revealed to be 0.4% (one abortion in 235 vaccinates) in one study.[12] This low – though not negligible – risk of undue harm may be considered an acceptable risk to some clients.

The administration of an MLV containing BHV-1 to pregnant heifers or cows that have not been previously vaccinated creates a high risk of undue harm. Prudence dictates that this practice is avoided. Yet, serendipitously, this practice will not yield detrimental results in situations where the pregnant heifers or cows were exposed to field strains of BHV-1 prior to the pregnancy – in which case the administration of vaccine was safe though unnecessary and unrewarding.

After an initial pre-breeding vaccination of heifers with one or two doses of MLV containing IBR and BVDV, revaccination either pre-breeding or during pregnancy with an MLV or killed vaccine according to label directions has been recommended as a reliable vaccination protocol. A prolonged randomized, controlled, clinical field trial did demonstrate the efficacy of administering two pre-breeding doses of MLV vaccine with annual revaccination using a combination vaccine containing a temperature-sensitive MLV BoHV-1 and killed BVDV to prevent fetal loss due to exposure to BVDV and BoHV-1.[13]

Conclusion

The thoughtful application of underlying principles combined with an understanding of the results of clinical trials can consistently result in the effective communication of clear, prudent and justified recommendations for practical vaccination protocols in beef cattle operations.

References

1. Falcone E, Cordioli P, Tarantino M, et al. Experimental infection of calves with bovine viral diarrhoea virus type-2 (BVDV-2) isolated from a contaminated vaccine. *Vet Res Commu.n* 2003;27:577-589.

2. Ellis J, Waldner C, Rhodes C, et al. Longevity of protective immunity to experimental bovine herpesvirus-1 infection following inoculation with a combination modified-live virus vaccine in beef calves. *J Am Vet Med Assoc.* 2005;227:123-128.

3. Ingelheim B. Express® Vaccines Now USDA-approved for Whole-herd Use. 2008; **https://www.thecattlesite.com/news/22268/express-vaccines-now-usda-approved-for-whole-herd-use**. Accessed 2/7/2025, 2025.

4. Aguilar JC, Rodríguez EG. Vaccine adjuvants revisited. *Vaccine.* 2007;25:3752-3762.

5. Hove P, Madesh S, Nair A, et al. Targeted mutagenesis in *Anaplasma marginale* to define virulence and vaccine development against bovine anaplasmosis. *PLoS Pathog.* 2022;18:e1010540.

6. Agency EME. Scientific conclusions and grounds to vary the marketing authorisations presented by the EMEA. 2000; **https://ec.europa.eu/health/documents/community-register/2000/200007103685/anx_3685_en.pdf**. Accessed 2/7/2025, 2025.

7. Houe H. Epidemiological features and economical importance of bovine virus diarrhoea virus (BVDV) infections. *Vet Micro.* 1999;64:89-107.

8. Zemjanis R. Vaccination for reproductive efficiency in cattle. *J Am Vet Med Assoc.* 1974;165:689-692.

9. Newcomer BW, Cofield LG, Walz PH, et al. Prevention of abortion in cattle following vaccination against bovine herpesvirus 1: A meta-analysis. *Prev Vet Med.* 2017;138:1-8.

10. Newcomer BW, Walz PH, Givens MD, et al. Efficacy of bovine viral diarrhea virus vaccination to prevent reproductive disease: a meta-analysis. *Theriogenology* 2015;83:360-365.e361.

11. Grooms DL, Bolin SR, Coe PH, et al. Fetal protection against continual exposure to bovine viral diarrhea virus following administration of a vaccine containing an inactivated bovine viral diarrhea virus fraction to cattle. *Am J Vet Re.s* 2007;68:1417-1422.

12. Ellsworth MA, Brown MJ, Fergen BJ, et al. Safety of a modified-live combination vaccine against respiratory and reproductive diseases in pregnant cows. *Vet Ther.* 2003;4:120-127.

13. Walz PH, Givens MD, Rodning SP, et al. Evaluation of reproductive protection against bovine viral diarrhea virus and bovine herpesvirus-1 afforded by annual revaccination with modified-live viral or combination modified-live/killed viral vaccines after primary vaccination with modified-live viral vaccine. *Vaccine.* 2017;35:1046-1054.