Vaccination protocols for beef calves

A. Woolums, DVM, PhD, DACVIM, DACVM
Department of Pathobiology and Population Medicine, Mississippi State University Mississippi State, MS 39762

Abstract

There are many vaccines to select from when vaccinating calves. No single vaccine protocol is appropriate for all operations; thus, vaccine protocol development requires understanding of the management of each operation. Unfortunately, published controlled field trials confirming efficacy of vaccines to prevent preweaning disease are rare, so protocols are often based on challenge studies or expert opinion. When vaccination of calves in the first 3 to 4 months of life is possible, vaccines for clostridial infections and respiratory viral infections are most likely to be used to limit preweaning disease. On some operations, preweaning vaccination may be delayed until close to weaning if the aim is to limit postweaning disease. Vaccines likely appropriate to limit postweaning disease include those for clostridial agents, agents that cause bovine respiratory disease, and agents likely to impact fertility in replacement heifers. Other vaccines may be appropriate on a case-by-case basis. Producers need to keep records of vaccine timing and disease in vaccinated calves, to help the veterinarian confirm efficacy of vaccine protocols. Veterinarians need to stay informed by periodically checking for new information on vaccine efficacy from systematic reviews, meta-analyses, or randomized controlled field trials testing vaccine efficacy against naturally occurring disease.

Introduction

Vaccination is one of the most common tasks veterinarians conduct or recommend. However, new graduates are often uncertain about which vaccines they should administer, and when recommended vaccines should be given. The large number of vaccines available for use in cattle, along with the relative lack of evidence-based guidelines for vaccine efficacy as vaccines are used in practice, contributes to confusion. This paper is intended to provide veterinary students with some guidelines regarding vaccination of beef calves prior to weaning, and suggestions about how to decide which vaccines to use in protocols for preweaning beef calves. This paper is a companion to another paper[9] also published in this Proceedings, so read both to get a more complete picture of things you should consider when vaccinating calves.

Why do we vaccinate?

Your first response to the question "Why do we vaccinate?" may be "To prevent infection" or "To prevent disease". But it's important to remember that challenge studies used to gain approval for currently marketed vaccines often do not demonstrate complete protection against infection, or even against disease, in all vaccinated cattle. In other words, for many of the vaccines commonly used, vaccination shortens the course of infection and decreases disease, but it does not completely prevent infection or disease in all vaccinated calves. See references 1, 2 and 4 of this paper as a few examples; many other studies have shown similar findings for a variety of vaccines. For endemic infectious agents associated with common disease syndromes like calf diarrhea or respiratory disease, you should get in the habit of thinking of vaccines as one of several tools that must be used together to optimally prevent illness and related production losses – and not as something that, acting alone, will always prevent infection or disease. The response of vaccinated individuals to disease challenge is not that "black and white". Vaccine efficacy can also be diminished in animals that are malnourished, already sick, or fighting off other infections – so in practice, there are multiple factors acting together that will determine whether vaccinated cattle get sick or stay healthy.

How do we know if a vaccine really works?

Vaccine efficacy is evaluated in research assessing immune responses in vitro, in experimental challenge studies, in randomized controlled field trials, and in systematic reviews and meta-analyses. The highest quality of evidence for any clinical practice is a systematic review or meta-analysis, which evaluates multiple randomized controlled field trials, so look for those studies when trying to make a decision about a vaccine to include in a protocol. However, in bovine practice, we often have to rely on experimental challenge studies to judge vaccine efficacy, because there are lots of experimental challenge studies (as they're required for vaccine licensure), and very few randomized controlled field trials (as they're risky, expensive and not required for licensure). More about sources of information regarding vaccine efficacy, and the quality of the evidence from these sources, is presented in the companion paper9 in this Proceedings.

Assessing challenge studies and field trials demonstrating vaccine efficacy

Veterinarians are often presented with data and other information from experimental challenge studies or, less commonly, randomized controlled field trials, to confirm vaccine efficacy. Push yourself to look at this information critically, and don't be intimidated by graphs or tables full of numbers. Interpreting data like this gets easier with practice. A few points to help you evaluate this information:

1) In an experimental challenge study, calves are vaccinated one or more times before being purposely exposed to one or more viruses or bacteria in the vaccine. The key feature of an experimental challenge study is that vaccinated animals, and unvaccinated "control" animals used for comparison, are purposely infected by the researchers. You will often be shown challenge study data by representatives from vaccine manufacturers to demonstrate the value of their vaccines.

   Challenge studies are required by the USDA Center for Veterinary Biologics to grant full approval of vaccines, so by definition, any fully licensed vaccine has been proven to be effective in a challenge study. But a challenge study is an artificial situation: the cattle are usually vaccinated when they have no serum antibodies to the vaccine, and when they are in a very controlled environment with little or no exposure to other problems occurring for cattle in "real life" – like competition for food, weather extremes,

or recent transport or co-mingling. Also, the method used to challenge cattle with the virus or bacteria, which must cause disease for vaccine efficacy to be tested, is also artificial – it's not the same as the way cattle are infected in "real life". So, a challenge study tells you what the vaccine can do in an ideal situation, but it doesn't represent very well the way vaccines are used on cattle operations.

To assess the importance and relevance of findings from a challenge study, ask yourself:

- Were cattle similar in age and breed to cattle you work with?
- Did disease occur after exposure in the control group? Did it look like naturally- occurring disease? Was disease less severe in vaccinated cattle?
- Was the vaccine administered in a way you would use it in the field? How much time elapsed between vaccination and exposure?
- Were statistically significant differences between vaccinates and controls found?
- Were statistically significant differences also medically important?

2) In a randomized controlled field trial, cattle, or pens of cattle, or farms, are randomly assigned to either be vaccinated, or not be vaccinated. The subjects of a field trial are cattle being managed on a farm in a typical production setting. After vaccination, cattle are monitored to see if naturally-occurring disease occurs, and differences in rates of naturally-occurring disease in the vaccinated cattle and in the controls are assessed after some time point. Other outcomes, like weight gain, or carcass characteristics at slaughter, may also be compared between the groups. **The key feature of a field trial is that disease in vaccinated animals and controls occurs only because of exposure to one or more infectious agents that the cattle acquire naturally.** No viruses or bacteria are purposely given to the cattle by the researchers.

Because field trials test vaccines in "real life" settings, they are a more meaningful test of whether a vaccine actually has a beneficial effect as it will be used in the field. Thus, a well-designed field trial is considered to provide higher quality evidence of benefit (or lack of benefit) of a vaccine than a challenge study. However, field trials are risky, because the researchers just have to wait for naturally-occurring disease to occur. If no disease occurs, then the research team can't tell if the vaccine is effective, and all the planning and sample collection to run the study is lost money and time. Also, because the cattle are in a "real life" setting, they are exposed to many other factors, in addition to vaccination, that might impact health – and so large numbers of cattle (many dozens to hundreds) need to be included in the study to identify effects of vaccination, which increases the cost of a field trial as compared to a challenge study.

To assess the importance and relevance of findings from a field trial, ask yourself:[6]

- Were the animals and management similar to my practice?
- Were concurrent (not historical) controls used? Were cattle randomly assigned to their treatment group so certain animals (like younger or smaller calves) were not systematically assigned to the vaccine or control group?
- Did disease occur in any group? Was the disease like that seen in my practice? How was disease diagnosed? If diagnosis was based on subjective clinical signs, were the people who identified disease unaware of the treatment allocation? This is very important to prevent conscious or unconscious bias that may lead to erroneous conclusions regarding vaccine efficacy.
- Were meaningful outcomes measured?
- Was protection against specific agents in the vaccine measured? Or was clinical disease the only outcome measured?
- Were there statistically and clinically significant differences between groups?

Vaccination of preweaning beef calves: Should we?

A list of currently available licensed vaccines available in the U.S. can be found at:

https://www.aphis.usda.gov/animal_health/vet_biologics/publications/currentprodcodebook.pdf

There are dozens of vaccines available for potential use in beef calves. Familiarize yourself with the products marketed by scanning catalogs or websites of retail sources of vaccines, or websites of the vaccine manufacturers – you may be surprised by the number of options. A list of the agents for which vaccines are currently available are presented in the companion paper[9] in this Proceedings, and some of these vaccines may be appropriate for use in preweaning beef calves.

Vaccinating preweaning beef calves is logistically challenging, because the calves are normally housed on pasture with their dams. Some confinement cow-calf operations exist, and in these situations, the logistical challenges are diminished. Because of the nature of typical cow-calf management, many cow-calf operations delay vaccination of calves until weaning. However, pre-weaning vaccination can be administered at two relatively convenient time points: 1) at birth, when some operations place ear tags, castrate male calves, and perform other interventions, or 2) at the age when calves are branded on some operations (60 - 90 days), and/or when cows are checked for pregnancy. A third option: on some cow-calf operations, calves are vaccinated at a pre-weaning time point, typically 30-45 days before weaning. The bottom line is that preweaning vaccination of beef calves usually needs to be done at a time when the cows and/or calves are being handled for some other purpose. The veterinarian thus needs to decide if vaccination at these time points makes sense – that is, is it likely to be safe, effective and cost-effective?

When considering the vaccination of preweaning beef calves, **decide whether the objective is to decrease disease in the preweaning period, postweaning disease or both.** For best effect, vaccines need to be given approximately a month before disease challenge is expected. Also, because of the immature immune response of calves, and the fact that some calves in a group may have concentrations of maternal antibody there are high enough to suppress vaccine response, it is ideal for preweaning calves to have two doses of vaccine before disease challenge is expected. All this means that, **if you are vaccinating to prevent preweaning disease, it may be necessary to administer two doses of vaccine to the calves, separated by a month or more, with the second dose given approximately a month before disease is expected.** Such a protocol is a lot of

work for the producer, because of the logistical issues mentioned earlier, and it carries the risk of injury to calves when they are removed from their dams and pushed into a chute for vaccination. Given this, only producers who have been troubled by substantial preweaning disease are likely to be willing to follow such a protocol. Anecdotal reports from producers to the author indicate that this type of protocol can be associated with beneficial reduction of disease in preweaning calves. But if preweaning disease is not a problem, then giving 2 doses of any vaccine to beef calves preweaning may not be warranted.

In cases where disease is occurring in the first month of life, the above recommendation to give 2 doses of vaccine separated by a month will obviously not be possible. The opinion of the author is that it is unlikely that vaccines can be used to control disease in the first month of life, simply because there is not time for a fully effective immune response to develop following vaccination. In such cases, it's likely better to focus on other measures to control disease, such as vaccinating cows a month or two before calving to increase specific antibody titers in colostrum, ensuring good colostrum consumption by calves, ensuring adequate nutrition of cows and heifers, preventing exposure of calves to cattle brought in from outside the farm or other regions of the farm, and maintaining a clean, uncrowded environment.

If vaccines are to be given to calves within the first week of life – such as at birth, on operations that handle calves at birth – intranasal vaccines may be more effective than parenteral vaccines, when that option is available, as they may be more likely to circumvent suppressive effects of very high concentrations of maternal antibody present in calves in the first week of life. While, as mentioned previously, vaccination at birth may not help prevent disease in the first month of life, it may provide priming to improve response to a booster given a month or two later. More research is needed to confirm the value of vaccination of beef calves on the first day or two of life.

In the specific case of calf diarrhea due to viral or some bacterial agents which is most severe in the first month of life, vaccination of calves is unlikely to be very helpful to prevent disease. Instead, vaccination of cows in late gestation, to increase concentrations of antibody to calf diarrhea agents in colostrum, is more likely to be effective. Of course, calves need to consume colostrum to receive this benefit. However, one of the limitations of vaccinating cows to prevent neonatal calf diarrhea is that colostral antibodies have their most important effect in the intestinal lumen, and after the cow is producing milk instead of colostrum, intestinal luminal antibodies may decrease to concentrations inadequate to prevent disease.[5] The limitations of vaccination to prevent calf diarrhea led to the development of management practices such as the Sandhills Calving System to more reliably prevent this problem.[7]

If preweaning calf vaccination is undertaken to prevent postweaning disease, then 1 dose of vaccine prior to weaning, with a booster given at or near weaning, is likely to be adequate in most cases. While more research specifically confirming this recommendation is needed, one helpful field trial determined that vaccinating calves at 67 days of age (branding age) and 190 days of age (weaning), or at 167 days of age (preweaning age) and 190 days of age, with a multivalent viral respiratory vaccine was equally effective for decreasing postweaning disease and improving some measures of production. Both protocols were associated with significantly improved outcomes as compared to no vaccination.[3] Thus this trial proved that it was possible to give calves a priming dose of vaccine at branding age or at preweaning age, with a booster at weaning, and realize benefits of vaccination with either strategy. More information about the factors that should be considered when developing vaccination protocols for preweaning beef calves are reviewed elsewhere in these Proceedings.[8]

Conclusions

Vaccination of preweaning beef calves may be beneficial, but the practice is labor intensive and carries some risk of injury to calves that must be separated from their dams for the practice. Therefore, vaccination of preweaning beef calves is most likely to be feasible when the cow-calf pairs are being processed for some other purpose, and the veterinarian must consider whether vaccination at such time points is likely to be beneficial for the operation. The small number of published randomized field trials testing the efficacy of preweaning beef calf vaccination means that it unclear whether preweaning vaccination is effective to control preweaning disease. Anecdotal reports from operations where preweaning pneumonia has been historically highly prevalent indicate that some producers have found preweaning vaccination to be useful to prevent preweaning pneumonia. To prevent preweaning disease, 2 doses of vaccine in the preweaning period may be necessary. There is more evidence supporting the value of preweaning vaccination to decrease postweaning disease, specifically, bovine respiratory disease; a single dose of vaccine given preweaning, with the booster occurring at or near weaning, can be beneficial.

References

1. Ellis J, West K, Konoby C, Leard T, Gallo G, Conlon J, Fitzgerald N. Efficacy of an inactivated respiratory syncytial virus vaccine in calves. *JAVMA* 2001;218:1973-1980.

2. Ellis JA, Gow SP, Mahan S, Leyh R. Duration of immunity to experimental infection with bovine respiratory syncytial virus following intranasal vaccination of young passively immune calves. *JAVMA* 2013; 243:1602-1608.

3. Kirkpatrick JG, Step DL, Payton ME, Richiards JB, McTague LF, Saliki JT, Confer AW, Cook BJ, Ingram SH, Wright JC. Effect of age at the time of vaccination on antibody titers and feedlot performance in beef calves. *JAVMA* 2008; 233:136-142.

4. Mahan SM, Sobecki B, Johnson J, Oien NL, Meinert TR, Verhelle S, Mattern SJ, Bowersock TL, Leyh RD. Efficacy of intranasal vaccination with a multivalent vaccine containing temperature-sensitive modified-live bovine herpesvirus type 1 for protection of seronegative and seropositive calves against respiratory disease. *JAVMA* 2016;248:1280-1286.

5. Parreño V, Marcoppido G, Vega C, Garaicoechea L, Rodriguez D, Saif L, Fernández F. Milk supplemented with immune colostrum: protection against rotavirus diarrhea and modulatory effect on the systemic and mucosal antibody responses in calves experimentally challenged with bovine rotavirus. *Vet Immunol Immunopathol* 2010;136:12-27.

6. Ribble C. Assessing vaccine efficacy in the feedlot, in Proceedings, 24th Annu Conf Am Assoc Bov Pract 1991; 137-141.

7. Smith DR, Grotelueschen DM, Knott T, Ensley S. Prevention of neonatal calf diarrhea with the Sandhills calving system, in Proceedings, 37th Annu Conf Am Assoc Bov Pract 2004;166.

8. Woolums AR. Immune management and vaccination of the preweaning beef calf, in Proceedings, 54th Annu Conf Am Assoc Bov Pract 2021.

9. Woolums AR. Vaccination protocols for dairy calves, in Proceedings, 54th Annu Conf Am Assoc Bov Pract 2021.

