Vaccines for all stages

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Abstract

There are many vaccines to select from when developing protocols for beef cattle operations, and no single vaccine protocol is appropriate for all operations. Thus, vaccine protocol development requires understanding of the management of each operation. Unfortunately, current field trials confirming efficacy of vaccines to prevent disease in "real life" settings are not common, and not all protocols have been tested. Thus, development of protocols for farm or ranch use often relies on experimental 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. Health records including vaccine timing and occurrence of disease in vaccinated animals can be a major help to confirm efficacy of vaccine protocols. Veterinarians should periodically check for new systematic reviews, meta-analyses, or randomized controlled field trials testing vaccines they used, to have the best information to use when planning vaccination protocols.

Introduction

There are numerous vaccines available to administer to beef cattle, and new graduates are often uncertain about which should be given, and when they should be used. Because vaccination is one of the most common practices directed by veterinarians, this situation contributes to confusion. This review is intended to provide new grads with some guidelines regarding vaccination of beef cattle, with suggestions about how to decide which vaccines to use. In most cases, new grads will start out using protocols recommended by more senior vets in the practice, but as a new grad gains knowledge and experience, they should be able to develop their own protocols for use on farms and ranches they advise. An excellent review[1] on vaccination was recently presented at another AABP Recent Graduate Conference, and readers interested in the topic of vaccination are encouraged to read that paper, too.

What is the purpose of vaccination?

Your first answer to the question "What is the purpose of vaccination?" 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 2-4 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, think 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. 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.

Do vaccines really work?

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 a lot of experimental challenge studies – they're required by the USDA Center for Veterinary Biologics for vaccine licensure – and very few randomized controlled field trials (because they're risky, expensive and not required for licensure).

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 follow.

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: 1) Were cattle similar in age and breed to cattle you work with? 2) Did disease occur after exposure in the control group? Did it look like naturally occurring disease? Was disease less severe in vaccinated cattle? 3) Was the vaccine administered in a way you would use it in the field? How much time elapsed between vaccination and exposure? 4) Were statistically significant differences between vaccinates and controls found? And were statistically significant differences also medically important?

In contrast to an experimental challenge study, 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] 1) Were the animals and management similar to my practice? 2) 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? 3) Did disease occur in any group? 4) Was the disease like that seen in my practice? 5) How was disease diagnosed? 6) 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. 7) Were meaningful outcomes measured? 8) Was protection against specific agents in the vaccine measured? Or was clinical disease the only outcome measured? 9) 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. Fortunately, the AABP has recommendations about vaccination which can be seen at **http://www.aabp.org/committees/resources/VaccGuidelines2021.pdf**.

Also, you should 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.

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 that is high enough to suppress vaccine response, it is ideal for preweaning calves to have 2 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 2 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 is probably not 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, 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]

Conclusions

Vaccination is one of the tools most used to help prevent many diseases. However, even in the controlled setting of the experimental challenge study, vaccines do not always prevent all infection, or all disease. Thus, it is important to understand that vaccines can help decrease infection or disease, but they must be used in conjunction with other practices to improve health and immunity, and decrease severity of challenge. There is no one protocol that fits all farms or ranches, and there are many cattle vaccines to choose from – so it can be difficult for new grads to decide what vaccines to use, and when. Initially, you will most likely use the protocols of more experienced veterinarians in your practice, but with time you should be able to develop protocols of your own for the practices you work with. New developments in vaccinology and immunology commonly occur, thus it is important to stay up-to-date with new information regarding vaccines and immunity in beef cattle by attending conferences and webinars. Remember that some sources of information have a vested interest in your purchase of vaccines, so pay attention and think critically when being presented with information about vaccines.

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