# Vaccination protocols for dairy calves

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## Abstract

There are many vaccines to select from when vaccinating dairy calves. No single vaccine protocol is appropriate for all operations; thus, vaccine protocol development requires understanding of the management of the dairy in order to assess the likelihood of various infections. Vaccines to limit the effects of clostridial infections, and respiratory viral infections, are most likely to be used in young calves. Vaccines to limit calf diarrhea are often used in cows to ensure high concentrations of passively acquired antibodies are present in the first 2 weeks of calf life. In older heifers, vaccines to prime resistance to agents that impact fertility or contribute to mastitis may be used. Other vaccines may be appropriate on a case-by-case basis. Producers need to keep records of which vaccines were given and when, and of which diseases occur in vaccinated calves, and when, to help the veterinarian confirm efficacy of vaccine protocols as used on each dairy. Veterinarians need to stay informed regarding which vaccines to recommend by periodically checking for new information 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 dairy calves, and suggestions about how to decide which vaccines to use in protocols for dairy calves. This paper is a companion to the paper "Vaccination protocols for beef calves" 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, again?

We vaccinate to prevent disease, right? Actually, vaccines for common endemic pathogens such as the viruses that cause calf diarrhea or respiratory disease do not prevent infection or disease of all animals in a vaccinated population, even when the vaccine is used correctly. Challenge studies used for approval – in some ways, the best case scenario for the vaccine – typically indicate that vaccination decreases disease severity and duration of pathogen shedding, but that it doesn't completely prevent infection or disease in all vaccinated individuals. See, for example, this paper's references 3, 4 and 5; many other examples are also available. Look at the data carefully in papers, presentations or webinars describing research testing vaccine efficacy, as you may sometimes find that the difference in disease severity, pathology or pathogen shedding between vaccinated animals and the unvaccinated control cattle is not as great as you are imagining, even when the differences are statistically significant. Pay attention to these details so you understand what vaccines are able to accomplish.

So, when we give vaccines for common endemic diseases, we can't expect to prevent all infection, or even all disease; we have to think of vaccination as one of several tools to use together to limit disease that makes cattle sick, and decreases their growth and productivity. Vaccination is less likely to be effective in malnourished animals, animals in an environment that is filthy, or in situations where cattle are overcrowded, or dealing with high rates of disease challenge.

## How do we know if a vaccine really works?

Vaccines are 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 the systematic review or meta-analysis, so look for those studies when trying to make a decision about a vaccination protocol. However, in bovine practice we largely rely on experimental challenge studies to determine vaccine efficacy, because many challenge studies have been conducted – because they're required for vaccine licensure. In contrast, few randomized controlled field trials testing efficacy, which are necessary to conduct systematic reviews and meta-analyses, have been conducted. Few systematic reviews are available because randomized controlled field trials are expensive, risky and not required for licensure. While challenge studies tell you what the vaccine can do in an ideal situation, they don't really represent the way vaccines are used in the field. More information on interpreting the results of experimental challenge studies and field trials is presented in the paper "Vaccination protocols for beef calves" in this Proceedings.

When evaluating a study or data regarding efficacy of a vaccine, consider the source: who paid for the research that led to the data? In veterinary medicine much research testing vaccine efficacy is funded by companies that make vaccines. Much of what we know about vaccines for use in cattle is because of company-funded research. However, it's important to remember the company that sells the vaccine has a vested interest in the vaccine being recognized as effective, and this could lead to bias in how research was conducted or presented. Watch out for that.

For veterinarians in private practice, rebates for purchase of vaccines may influence decisions about which vaccines to use; think about the impact of this, and how this might bias your vaccine protocol development.

Keep up with the current literature. Go to meetings and ask questions. Be skeptical. Ask to see the data.

## Which vaccines should we give?

There are MANY vaccines available for possible use in cattle, coming from different manufacturers, containing different infectious agents in different combinations. Familiarize yourself with the different options by scanning catalogs or websites from companies that sell vaccines. When selecting vaccines, a veterinarian must decide whether to recommend modified live

  

or inactivated, intranasal or injectable, commercially available or autogenous. In practice, after graduation you will likely begin by recommending vaccines as your employer does, then modifying your approach as you see how this works, and learn more.

For dairy calves in the first 60 days of life, vaccines to limit disease due to clostridial infections and respiratory viruses are the most likely to be appropriate. Vaccines to prevent calf diarrhea are best used in cows, so that calves have high concentrations of protective antibody in the first 2 - 4 weeks of life, when infections by these agents are most likely to cause serious disease. Remember there are no vaccines for some important causes of calf diarrhea, such as cryptosporidiosis, so good nutrition and hygiene are a must to limit calf diarrhea, vaccination alone will not prevent all disease.

When vaccinating for respiratory viruses, possibly suppressive effects of maternal antibody can be especially relevant in the first month of life, and priming (first) doses given by the intranasal route may be most effective in calves in this age group.

Unfortunately, for those who like simple answers, there is no one vaccination protocol that can be recommended for all dairies. Development of a vaccine protocol requires that the veterinarian understands the management of the dairy well enough to know which infections are likely. The veterinarian also needs to know whether effective vaccines are available to decrease the rate of likely infections and resulting disease, and whether such vaccines can be applied effectively on the dairy, given the dairy's management constraints.

The AABP is in the process of developing recommendations for vaccine use in cattle, and these should be helpful – they're intended to be – but they will probably be at least somewhat controversial, and they will require periodic review and revision as more is learned about efficacy and the risks and benefits of available vaccines. Bottom line: you'll have to keep learning about vaccines available for cattle for the rest of your career in order to make good recommendations for vaccine use.

## Available vaccines to consider using in dairy calves

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**

Specifically, at this time, vaccines are commercially available for the following agents:

- **Enteric diseases:** enterotoxigenic *E. coli*, rotavirus, coronavirus, *Salmonella sp.*, *Clostridium perfringens* type A or types C and D.
- **Respiratory diseases:** infectious bovine rhinotracheitis virus (IBRV), bovine respiratory syncytial virus (BRSV), parainfluenza type 3 virus (PI3V), bovine viral diarrhea virus 1 and 2 (BVDV1 and BVDV2), *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, *Mycoplasma bovis*.
- **Reproductive diseases:** IBRV, BVDV1 and BVDV2, *Camplylobacter fetus-jejuni*, *Leptospira* (various serovar combinations), *Brucella*
- **Mastitis:** lipopolysaccharide core antigen vaccines, *E. coli*, *Klebsiella pneumoniae*, *Staph. aureus*, *Strep. uberis*
- **Miscellaneous:** multivalent clostridial vaccines in various combinations, *Moraxella bovis* (pinkeye), rabies, wart vaccine

One or more of the vaccines listed above are likely appropriate for use on all dairies. Some vaccines listed above may never be appropriate for use. To make a final decision of whether to add a specific vaccine to a farm protocol, look for published systematic reviews/meta-analyses[6] or randomized controlled field trials,[7] or challenge studies[3-5] or summaries of expert opinion,[1] if systematic reviews or randomized controlled field trials are not available. Also, talk to 1 or 2 more experienced veterinarians who work with cattle similar to those in your practice. An excellent review recommending example vaccination protocols that can be applied to dairy calves and heifers, with background for these recommendations, has recently been published.[2]

## How can we tell if vaccination we recommend is working?

Encourage producers to keep records of what vaccines are given and when, and to which cattle, and when cattle are treated for disease, and what disease they're treated for. Lack of records of these activities is common on U.S. cattle operations, and if there are no records, you really have no idea of what is happening. And if your producers keep records, prioritize finding time to look at them. Simple outbreak curves graphing the number of cases per day or week over time can provide a visual representation of disease that may help to identify things that are working – or not working – to limit disease.

Find benchmarks for different common diseases to get an idea of the how much disease occurs in "average" production settings, and use this to compare disease rates in the dairies you advise. Surveys by the United States Department of Agriculture National Animal Health Monitoring Service (NAHMS) are one good source of such information:

**https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/monitoring-and-surveillance/nahms**

Necropsy animals that die. Necropsies of food animals are usually at least partially subsidized at state veterinary diagnostic laboratories, so this is a relatively cheap way to survey for causes of disease on operations. Anecdotal reports from veterinarians in practice indicates that some diagnostic laboratories, or perhaps some diagnosticians, are better than others at providing useful information from necropsies of calves or cattle. Start with your state diagnostic lab, but if after a few cases you don't feel like you're learning much from the interaction, it may be more fruitful to do the necropsy yourself and send samples to another state lab. Generally speaking, when it comes to livestock, diagnostic labs in states that have large populations of the species in question often offer a wider variety of tests, and may have diagnosticians with more experience relevant to your problem, as compared to diagnostic laboratories in states with relatively small populations of the livestock species in question.

Microbiologic and serologic testing to identify infectious agents, or to measure antibodies to infectious agents, may seem like a good way to tell if vaccination is working, but BEWARE: this kind of sampling is not always as helpful as you may think. The timing of collection of samples is important to the relevance of the findings, and the results need to be considered in light of the time between vaccination and sample collection. It may be helpful to contact a specialist in microbiology, immunology or epidemiology before undertaking large scale testing, in order to develop a sampling plan, and to gain assistance in interpreting the results of testing.

  

Before sending samples for diagnostic testing the first time: review the lab's website, or call the lab, to confirm how to collect, store and ship the samples. This can make a lot of difference in whether you get useful information from testing. Otherwise, you may spend hundreds of dollars of the client's money and have nothing to show for it. Embarrassing.

## Vaccination can't hurt, right?

Vaccination is not innocuous. Some adverse consequences of vaccination that are always possible, with decreasing likelihood, include local inflammation or infection, generalized cellulitis, and lethal anaphylaxis. If you vaccinate animals, have a bottle of epinephrine available in case a vaccinated animal develops anaphylaxis that requires treatment, and don't leave the farm until it's been 30 minutes since the last animal was vaccinated, which gives time for immediate hypersensitivity reactions to occur. Some systemic reactions occurring within minutes of vaccination are due to an inflammatory reaction to endotoxin in the vaccine ("endotoxic shock"), which results from a different mechanism than anaphylaxis, but which may look clinically similar. Endotoxic shock is best treated with flunixin meglumine and possibly fluid therapy.

Some vaccines can induce abortions, and if a cow aborts her calf, productive months of her life are lost. A vaccine that induces a useful immune response also induces inflammation; in fact, a vaccine that induces no inflammatory response probably isn't inducing much of an immune response. However, that inflammatory response may cause a dairy cow to decrease milk production for one or more days; if this happens in hundreds of cows at one time, that can lead to a noticeable negative effect on the milk check.

Presumably, because dairy calves are easy to access compared to beef calves, they are sometimes given relatively large numbers of vaccines in the first year of life, to a degree that can seem excessive. Because vaccination demands protein, energy, vitamins and minerals for expansion of the immune response, it exerts a metabolic cost. Large numbers of vaccines given in a short period of time may be more costly, metabolically speaking, than some of the vaccines in the protocols are worth. Unfortunately, we don't have many data on the actual metabolic cost of various vaccination protocols, and the financial cost of this metabolic cost, so it's difficult to make a general statement about how much vaccination is too much…but keep in mind that it is possible to vaccinate too much. More is not always better, and fewer, but more properly timed vaccines may be more effective than more vaccination.

Vaccination is one of the great advances of medicine, and when used appropriately, in combination with sensible biosecurity and good husbandry, vaccination can be health- and life-saving. But vaccination should be a considered activity: you should stop and consider the pros and cons before giving any vaccine, and make sure you can make a case for the pros outweighing the cons.

## Conclusion

Many vaccines exist which may limit disease in dairy calves. There is no single vaccination protocol that can be recommended for every dairy. Knowledge of the farm management and disease risk is necessary to develop rational vaccine protocols. The paucity of randomized controlled field trials testing vaccines as used in the field currently limits the ability of veterinarians to use high quality evidence to make decisions about which specific vaccines should be included in protocols. In the absence of such high-quality data, data from challenge studies and summaries of expert opinion may be used. Encouraging producers to keep records regarding when vaccines are administered, and when vaccinated calves are treated for disease, may help the supervising veterinarian determine whether vaccine protocols are having the desired effect to decrease disease and maintain health, growth, and productivity on dairies they advise.

## References


1. Chamorro MF, Palomares RA. Bovine respiratory disease vaccination against viral pathogens: modified-live versus inactivated antigen vaccines, intranasal versus parenteral, what is the evidence? *Vet Clin North Am Food Anim Pract* 2020; 36:461-472.

2. Chase C. Practical immunology and beef and dairy vx protocols: starting from ground zero--what,when and how, Proceedings, Am Assoc Bov Pract Recent Graduate Conference 2021; 10-18.

3. 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.

4. 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.

5. 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.

6. Theurer ME, Larson RL, White BJ. Systematic review and meta-analysis of the effectiveness of commercially available vaccines against bovine herpesvirus, bovine viral diarrhea virus, bovine respiratory syncytial virus, and parainfluenza type 3 virus for mitigation of bovine respiratrory disease complex in cattle. *JAVMA* 2015; 24:126-142.

7. Windeyer MC, KE Leslie, SM Godden, DC Hodgins, KD Lissemore, SJ LeBlanc. The effects of viral vaccination of dairy heifer calves on the incidence of respiratory disease, mortality, and growth. *J Dairy Sci* 2012; 95:1-9.


  