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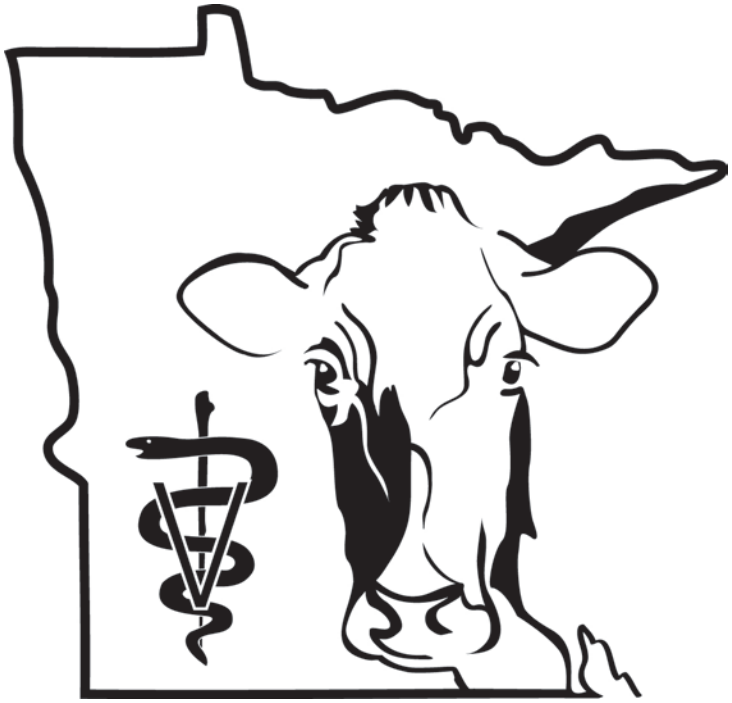

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Designing Vaccination Programs for Today's Cattle

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INTRODUCTION

In order to scientifically choose a vaccine or design a particular vaccination program it is necessary to consider many variables. Some of these include:

1) Presence and degree of challenge of the particular diseases on the farm or ranch.
2) Management practices available that lend themselves to vaccination programs.
3) At what times or ages are the disease problems occurring and are they associated with any stressor?
4) How the disease is protected against by the body.
5) Some basic immunology concepts.
6) The information that is available on products being considered and the source and quality of the information.

CHALLENGE

One thing to keep in mind is that challenge and protection are in a constant state of fluctuation. We like to think that when we vaccinate an animal, they all develop a certain level of protection. However, biological variability affects the level of protection. The same is true with the amount of exposure to a pathogen. Overwhelming challenges can override the immunity and lead to disease in vaccinated animals.

TIMING OF DISEASE

Many of the farms we work with will have a consistent time when certain diseases occur. The timing may give some insight into stresses that are occurring in the management of the cattle that can be dealt with and have more of an impact than vaccination. Furthermore, this type of a history is helpful to determine the timing of vaccinations. This is a tool that is often underutilized in veterinary medicine but if we know when a problem is occurring pre-vaccination schedules that will give maximum immune responses close to the expected trouble time can be very beneficial.

ASSESSING VACCINE EFFICACY

Vaccine efficacy can be extremely difficult for the practitioners to assess. Traditionally we have been shown serologic data showing pre and post vaccination titers. This increase in titers was then equated to protection. For many diseases there is a poor correlation between an antibody being measured and the protection generated by the vaccine in the animal. Recently the addition of cell mediated immune function tests have been added to show a more complete stimulation of the immune response. Although this does give more information on the vaccine it still does not answer the basic questions of how well a vaccine really protects. This can only be answered by actual good challenge studies. In order to assess a challenge study the following information is needed:

1. trial design including animal characteristics
2. statistical analysis of the results
3. route of administration of the challenge
4. the method for clinical score assignment
5. publication of the results in a peer reviewed article

Unfortunately for many of our diseases, the challenge model is not well established. This is a major shortcoming of many vaccine efficacy trials. Field trials are even harder to assess but are valuable at answering the effectiveness and efficiency of vaccines (i.e. the efficacy in a particular situation). An article by Ribble gives a good overview of field trial analysis and should be considered as a reference. The concept of herd immunity becomes very important as we design field efficacy trials and must be considered when you assess field trial data.

MODIFIED LIVE VERSUS INACTIVATED VACCINES

There are basically three different technologies available today in cattle viral and bacterial vaccines. The development and manufacture of these types of vaccines is very different since the composition of the vaccine itself is so different.

a. Modified live (attenuated) vaccines contain living bacterial or viral organisms. They are usually collected from a field disease and then grown in abnormal host cells (viral) or media (bacterial) to change or attenuate the pathogen. Each time the pathogen is grown through a replication it is called a passage and it is administered back to the animal to see if it can still cause disease. After several passages the pathogen will begin to lose virulence factors since it cannot cause "disease" in this unnatural host cells. Once the pathogen can no longer cause "disease" in the target species it is then tested to see if it can confer protection. The final vaccine is usually passed a number of times beyond the passage where virulence is no longer seen to decrease the risk of reversion to virulent pathogen.

b. Inactivated (killed) vaccines are easier to develop since virulence is not a problem. The same pathogen is isolated form a disease outbreak. The pathogen is grown and then chemically or physically killed. The inactivation is usually achieved by either adding a chemical

to the pathogens or using ultraviolet rays. The major concern with inactivation is the potential loss of important epitopes. An adjuvant is normally added to inactivated vaccines to heighten the immune response. The vaccine is then tested for efficacy.

c. Genetically engineered vaccines have been altered genetically usually through a mutation. This mutation may be induced by several different methods but the ensuing bacteria or virus has different properties that may alter virulence or growth characteristics. These types of vaccines are usually considered to be modified live (although inactivated marker vaccines fall into this category). Examples include temperature sensitive viral vaccines, streptomycin dependent Pasteurella hemolytica and gene deleted IBR vaccines.

Once this efficacy has been established, then the vaccine is put through a series of experiments to determine the minimum dose required to give adequate protection (MID). The vaccine will contain more than the MID in order to obtain the dating on the label.

DESIGNING A VACCINATION PROGRAM

Vaccination programs in a cow herd need to be custom designed for the particular need of the herd. Vaccination programs in the replacement stock have two specific goals that need to be met. The first is to prepare the calf against any pathogens that are causing disease problems in the calves. The second is to prepare the calf for entry into the adult herd with a good foundation of protection from which to build herd immunity. Although herd programs vary in pathogens contained for most cow/calf and dairy herds the minimum vaccination program should be built around the four major viral diseases (BVD, IBR, P13 and BRSV) the five Leptospira serovars and for most parts of the country the major Clostridial diseases and Brucellosis. This should be the cornerstone of the program other pathogens are then optional and are added depending on herd or area problems. At least one four-way modified live viral vaccine should be included for replacement animals to establish a strong baseline immunity against BVD and IBR.

BOOSTER IMPORTANCE

It is important to follow the label directions for administering vaccines. Killed vaccines and modified live BRSV require a booster before protection is complete. The first time a killed vaccine is adminstered the primary response occurs. This response is fairly short lived and is not very strong. The predominant antibody is IgM. The response seen after a booster vaccination is called the secondary response or anamestic response. This response is much stronger and long lived and is primarily IgG. Also, there is more memory made in response to the booster. If the booster is given too early, the anamestic response doesn't occur; and if too much time elapses before the booster is given, it acts as a primary shot not as a booster. With modified live vaccines, the primary shots also stimulates the secondary resonse without needing a booster since the virus or bacteria is growing in the animal.

ADVERSE REACTION

Adverse reactions are a potential risk with any vaccination used. These reactions fall into three primary types:

1. Immediate hypersensitivity is mediated by IgE and the release of granules from basophils and mast cells. This reaction is seen within minutes of vaccination and often begins with shaking or sweating. The majority of these animal respond very well to epinephrine.

2. Delayed hypersensitivity is mediated by a subset of T cells and is delayed by up to 24 hours following vaccination. The signs are similar to immediate hypersensitivity and treatment is again epinephrine.

3. One of the more common reactions seen in dairy cattle has been associated with the endotoxin found in some vaccines. This is seen primarily in Holsteins due to some genetic predispositions and can be seen following administration of any gram-negative bacterin. The pre-breeding yearling heifer appears to be the most sensitive. The signs seen vary depending on farm or individual sensitivity and/or the number or severity of the gram negatives in the vaccination program for the day and include:

a. anorexia and milk drops
b. early embryonic deaths
c. abortions
d. gram negative bacterial (endotoxic shock), requiring steroids, antihistamines and fluids

SUMMARY

Designing a vaccination program involves a good history of the individual farm as well as a basic understanding of the immune system. The vaccines chosen should have good solid efficacy studies as well as effectiveness and efficiency studies if possible to ensure that the product can fulfill the needs of the farm or ranch. Management decisions may be made that do not maximize the potential of the products chosen and realistic expectations of all products should be well explained to the producer before they are used. The owner should be involved in the vaccine decision process so that all the information on the product is shared. The establishment of good baseline immunity of replacement heifers and the foundation vaccination program can determine much of the replacements future health status and should be stressed in vaccination programs.

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