

## TIMING OF VACCINATION IN BEEF CATTLE HERDS

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Infectious reproductive diseases have great potential to create significant damaging effects to reproductive efficiency and therefore profitability for the beef herd. Pathogens causing reproductive diseases include: bovine viral diarrhea (BVD), infectious bovine rhinotracheitis (IBR), *Leptospira*, *Tritrichomonas foetus*, *Campylobacter fetus* subsp. *venerealis* (“vibrio”) and *Neospora caninum*, among others. Management practices to prevent or control infectious disease should consist of efforts directed towards biosecurity (keeping sources of new diseases out of the herd), environmental control (reducing stress and conditions in which infectious diseases may be transmitted), and vaccination.

Vaccination has long been employed as a means to increase the resistance of individuals, thereby the group, to infectious agents. For reproductive diseases, the goal is to increase resistance of the female (or bull) toward agents that will adversely affect the female’s ability to carry a pregnancy to term, the hopeful result of which is a healthy, viable calf. The focus of many reproductive vaccine programs is on preventing abortions, but attention should also be paid to diseases that have an affect on ovulation rates, fertilization rates, embryonic survival rates, and perinatal survival rates. Many agents of reproductive diseases will have effects on several, if not all, of these stages of reproduction.

In most cases in which vaccine is used as a management tool to lower the risks or effects of disease, the focus is on protecting the individual animal from illness that has an economic effect. For reproductive diseases, this focus shifts to protecting the pregnancy. In mature cattle, most agents of reproductive disease will cause very little to no clinical illness in the cow, yet in some cases may easily infect the reproductive tract or developing fetus such that infertility is the result. For example, an exposure of a pregnant cow to a relatively moderate amount of BVD virus may result in no outward signs of illness in the cow, yet be enough to cross the placenta and infect the developing fetus, with several potential deleterious outcomes.<sup>1</sup>

Reproductive diseases for which vaccines are widely used and available have been described in the previous paper. With the possible exception of *Neospora caninum*, all of these agents have been implicated in failure to conceive or early embryonic death, resulting in open cows at pregnancy examination. Therefore, a reproductive vaccine program should be designed to confer high levels of immunity at the time of breeding and in early gestation. Because most vaccines take two to four weeks to reach peak effect, vaccination should be performed well before breeding time, optimally 28–30 days pre-breeding.

## **Vaccination Prior to Breeding and/or Synchronization**

In intensively managed herds, especially those that employ estrus synchronization protocols, operators are faced with running cattle through the chute several times to accomplish the necessary injections and treatments required by the synchronization program. Since every trip through the chute results in potential stress for the breeding animal, and increased time and labor commitments for the producer, a common question is whether pre-breeding vaccinations can be performed at the same time as estrus synchronization.

To answer that larger question, two smaller questions must be answered first: 1) Will the vaccine work quickly enough to protect the female at breeding time and early gestation? and: 2) Will the vaccine itself (especially a modified-live vaccine) cause reduced pregnancy rates or harm the effectiveness of the synchronization program?

### **1. Onset of action of vaccines.**

The onset of action of most vaccines depends on the type of vaccine (killed vs. modified live) and prior immunity or vaccination. As a general rule, modified live vaccines have a quicker onset of action than killed vaccines. Cattle that have been previously exposed to the vaccine strains will see a more rapid effect from the vaccine than cattle encountering the vaccine for the first time.

Moreover, even in the case in which a modified live vaccine is used in a previously vaccinated animal, there still is a “waiting period” in which the body responds to the vaccine. This period still may be as long as several days. Therefore, if an animal encounters a large exposure to the disease agent at breeding time, the female’s immunity still may not be ramped up enough to effectively protect the cow and her reproductive tract from the encounter.

### **2. Will the vaccine itself result in reproductive failure or reduced success of synchronization?**

Several studies have outlined the effects of IBR virus--both wild strains and modified live vaccine strains--on the ovaries and reproductive tract of females in and after estrus. Three of these studies<sup>2,3,4</sup> showed that destruction of ovarian tissue occurs when seronegative calves (calves presumably not previously exposed to IBR) were inoculated intravenously or intramuscularly with either wild virus or MLV vaccine virus during or immediately following estrus. Two other similar studies<sup>5,6</sup> showed decreased pregnancy rates after IV<sup>5</sup> or IM<sup>6</sup> injection of MLV IBR vaccine to seronegative animals. It is important to note that heifers in these studies were naïve to the IBR virus (had no prior immunity) and that in the case of the studies evaluating pregnancy rate<sup>5,6</sup> small numbers of animals were used to draw the conclusions reached. These studies, taken together, provide ample evidence that **naïve heifers** should not be given MLV vaccines containing IBR virus at estrus.

Home-raised replacement heifers and mature cows on many operations will, however, have had previous exposure to vaccine virus strains. What effect does MLV IBR vaccine have on those animals? Four studies evaluated the effects of MLV vaccination around the time of breeding on subsequent conception and/or pregnancy rate on populations of animals that had previously had vaccine. Stormshak, et al<sup>7</sup> compared animals vaccinated with MLV

multivalent vaccines 30 d. prior to breeding with animals vaccinated 9 days prior to breeding (at the same time as synchronization with Synchronrate-B®). No differences between groups were found for first-service conception rate or overall pregnancy rate, indicating that vaccination at the time of estrus synchronization in that program had no detrimental effects. This population consisted of yearling crossbred ranch heifers in which prior vaccination status was not mentioned in the study.

Donovan, et al<sup>8</sup> described a group of previously vaccinated Holstein heifers in which vaccination 21 days or less prior to insemination with a multivalent MLV vaccine actually resulted in a **positive** effect on first service conception. Rosenberg<sup>9</sup> and Whittier et al<sup>10</sup> report a study in which previously vaccinated animals were given multivalent MLV vaccine either 30 days prior to insemination or at the initiation of estrus synchronization. Synchronization consisted of a CIDR®-Co Synch program in which the vaccine and initial dose of GnRH were both given on day 1 of the protocol. No differences were found between the vaccine groups on conception rate to timed artificial insemination or overall pregnancy rate.

These studies indicate that previous vaccination with MLV vaccines may enable producers to combine MLV boosters with estrus synchronization. In summary, these important points should be noted:

1. Studies using naïve or seronegative heifers showed detrimental effects from using MLV vaccines around the time of estrus in those animals. Animals that have never received prior vaccination, or animals of unknown vaccination status should be given MLV vaccine well in advance (30 days or more) of synchronization or breeding.
2. Even in previously vaccinated animals, the timing may not be right for giving MLV vaccines at estrus synchronization or breeding. Even booster doses of vaccine need several days for peak effect. Administering the booster at the time of estrus synchronization or breeding may not give peak protection to a disease challenge during early gestation.

### **Vaccinating Pregnant Cows**

In recent years, several vaccine manufacturers have begun marketing their MLV vaccines as approved for administration to pregnant animals. This recommendation is given with the caveat that animals must have been properly vaccinated pre-breeding with the same MLV vaccine. This is designed to appeal to producers who are only able to vaccinate their cows during pregnancy, for example, at preg-check time--although for at least the first season they must work the cows and vaccinate before the breeding season.

While a convenient prospect for some producers, this practice is less than optimal for several reasons. First, as mentioned previously, many if not all reproductive diseases have manifestations early (first two months or earlier) in gestation. In the case of a typical upper Midwest cow herd that starts their breeding season in early July, vaccinating at preg-check time may, for example occur in November, at which time the fetus is in its third or fourth month of development. If optimal immunity from the booster occurs two to four weeks

following the vaccination, it will be a full seven months (from December to July) after peak immunity when the greatest threat to reproductive health would occur (breeding and early gestation). For this reason, gestational reproductive vaccine programs lack optimal timing.

Because MLV IBR vaccines have demonstrated the potential to induce abortions in pregnant animals, this practice must be approached with extreme caution and only with the guidance of a veterinarian. It should be noted that vaccines which have indications for pregnant cow administration on their labels have passed at least the minimum safety requirements as put forth by FDA. However, studies undertaken to meet these requirements may or may not be applied to populations of animals that represent the range of body condition, health, and nutritional status present in the typical beef cow herd. Perhaps the actual wording from one of these vaccine's labels underscores this most accurately: "Fetal health risks associated with the vaccination of pregnant animals with modified live vaccines cannot be unequivocally determined by clinical trials conducted for licensure"!

SDSU's diagnostic laboratory has experienced an increase in diagnosis of abortions due to IBR. For the period encompassing July 2005 to June 2006, 17 cases were diagnosed with IBR abortion. This compares to between 3 and 9 cases diagnosed in each of the previous five years. In nine cases (representing 3 herds) of the seventeen 2005-06 cases, MLV vaccine given during gestation was mentioned in the history provided.

For these reasons, the following recommendations regarding the use of MLV vaccines during pregnancy are in order:

1. When using MLV vaccines in pregnant animals, the product label **must be followed to the letter**. If animals have not previously been vaccinated pre-breeding during the same year or the first year of the program MLV vaccines **should not** be given to the animals. For example, one vaccine label explicitly states that the previous dose of vaccine must have been given within the past 12 months. If **any** amount of time has elapsed past this 12-month period, the pregnant animals should **not** be vaccinated with an MLV vaccine.
2. **Only healthy animals** in the proper plane of nutrition and body condition should receive the labeled vaccine regimen.
3. Purchased bred cows or bred heifers should be considered **naïve** animals not previously vaccinated in the spring unless there is rock-solid proof that they have. Producers with the best of intentions can still improperly communicate the brand of vaccine used and the timing of administration. Vaccinating naïve pregnant animals will result in a significant at best, and devastating at most, loss of pregnancy.

### **Proper Pre-conditioning**

We have seen from the discussion above that a proper pre-conditioning, or pre-weaning vaccination program is critical to the safety and effectiveness of future vaccination programs especially when placed in the context of vaccinating animals close to the time of estrus synchronization or breeding, and during gestation. **Proper pre-breeding vaccination begins before the heifer calf is weaned.**

Replacement heifer calves should receive a dose of multivalent (IBR-BVD-PI3-BRSV) viral vaccine prior to weaning and again at or around weaning time. In addition, vaccination with *Leptospira hardjo-bovis* should occur at this time for females identified as replacement candidates. This is due to the fact that young calves are exposed to this reproductive pathogen early in life, and delaying vaccination until adulthood generally will not be of use in an animal that is already infected.

Proper pre-conditioning use of reproductive vaccines is the best way of ensuring that boosting these animals prior to breeding will result in 1) optimal immune response, and 2) optimal safety for the reproductive cycle and developing pregnancy.

### **Conclusions**

1. Replacement heifers should be properly vaccinated pre-weaning and at weaning with either modified-live or killed viral vaccine. Currently differences of opinion exist among veterinarians as to the merits of both types of vaccines. Both types have strong opponents and advocates, but it appears that modified-live vaccine programs are more predominantly used than killed viral vaccine programs due for the most part to completeness of immune response. At the same time, replacement heifers should receive a dose of *L. hardjo-bovis* vaccine both pre-weaning and again at weaning.
2. All replacement heifers and cows should be boosted with multivalent viral plus lepto (including *L. hardjo-bovis*) 30 days prior to breeding. For herds using natural service, *Campylobacter fetus* subsp. *venerealis* (“vibrio”) should also be included.
3. If MLV vaccine must be given less than 30 days before breeding, it should be given as soon as possible, and then only to animals known to have had the proper pre-conditioning regimen of preweaning and weaning vaccinations. Under no circumstances should MLV vaccines be given after breeding.
4. Using reproductive vaccine at preg-check time is less than optimal. Modified live virus vaccines during pregnancy should only be given to animals of known prior (pre-breeding) vaccination status, and then **only** with strict adherence to label directions.

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