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HOW TO GET THE MOST OUT OF YOUR VACCINATION PROGRAM

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Introduction

This paper provides some general recommendations on vaccination and also provides additional comments on the use of viral vaccines in pregnant animals and at synchronization plus the 1mportance of timing for good colostrum development.

Cattle Vaccination Programs

There is no "single vaccination program" that will work on most farms. Each farms' programs needs to be based designed based on the actual threats and needs of the farm and not based on a company's or neighbors suggested program. The generic disease syndromes (respiratory, reproductive or enteric) included in this sample vaccination program are provided as examples and vaccines for specific diseases should be those that are either present (and/or have been a problem in the past) and/or a new disease that is a real threat to the farm.

CATTLE VACCINATION PROGRAM

Beef

Heifers (Prebreeding) Heifers need to receive at least one dose of MLV prior to addition to the breeding herd

Respiratory and Reproductive Diseases

MLV-2 doses

>6 months of age and repeated 2 months before breeding

Inactivated-2 doses

5 weeks and 2 weeks before breeding

Enteric Diseases

MLV-2 doses

5 weeks and 2 weeks before calving

Inactivated-2 doses

10-12 weeks and 4 weeks before calving

Cow Herd

Respiratory and Reproductive Diseases

Inactivated

3-4 weeks before breeding- ideal

MLV

3-4 weeks prior to breeding-ideal. Do not vaccinate pregnant cows- no efficacy demonstrated for preventing PI in subsequent pregnancy- Problems with IBR abortion in animals poorly vaccinated

Enteric Diseases

MLV-1 doses

2-4 weeks before calving

Inactivated-1 dose

4-6 weeks before calving

Calves (<4 months)

Respiratory and Reproductive Diseases

MLV

Calves on Vaccinated Cows-MLV Intranasal vaccines (Depends on Maternal Antibody levels-MANY MLV IM or SC **NOT EFFECTIVE**-ONLY adjuvanted MLV IM or SC)

Inactivated- Well adjuvanted, not affected by Maternal Antibody

Calves (>4 months)

Respiratory and Reproductive Diseases

2-3 weeks prior weaning

MLV-1 dose

Inactivated-2 doses

At weaning

MLV-Immunosuppressive

Inactivated-2 doses

2-3 weeks post weaning

MLV-1 dose

Inactivated-2 doses

Vaccination and Viral Reproductive Diseases

Both bovine viral diarrhea virus (BVDV) and infectious bovine rhinotracheitis virus (IBRV) can cause reproductive issues. Work with BVDV MLV vaccines has shown that BVDV can infect the ovary. This vaccine virus has not been shown to continue to replicate and its exact effect is unclear. On the other IBRV can cause though is when the virus infects the cow and gets in the bloodstream. Normally IBR infections occur as oral and upper respiratory infections that may or may not get into the blood stream. With parenteral MLV vaccines the virus always has the opportunity to get in the blood stream. There is no danger of inactivated vaccines causing this problem. Once in the blood stream the virus can affect reproductive organs and in particular the ovary. The ovary is the major target and the virus has major effects on both the corpus luteum and developing ovarian follicles. In the normal reproductive cycle the cow's ovary will have two follicular waves where a primary follicle will develop in each wave. In the first wave, the primary follicle regress but after the second wave that follicle matures and an egg is released. The second follicle that released the egg then becomes the corpus luteum. The

corpus luteum (or CL) is essential for the early maintenance of pregnancy. IBRV can also infect the fetus directly and cause abortion. There is no danger of inactivated vaccines causing this problem. The safest approach when vaccinating pregnant cows is to use in activated vaccines.

Vaccination and Synchronization

Work by Van Der Maaten and Miller from 1985 (1) where IBRV was administered the day after breeding showed a variety of effects of IBR. They used the Colorado or Cooper strain used in many MLV vaccines. They harvested the tissue from the heifers, 11- 15 days after infection. The most dramatic effect was on the corpus luteum. The corpus luteum or CL is the structure that is formed in the ovary after the animal ovulates. IBRV homes to the ovary and causes necrosis of the corpus luteum. This causes disruption of the estrus cycle. The virus also can infect the developing ovarian follicle, which will have a negative effect on the next estrus cycle. From a study that we have completed and is in press (2), we found that MLV vaccines had a dramatic effect on progesterone and estradiol and most importantly on conception. The negative effect on conception has been known for over 20 years because of the effect that IBRV has on the CL. With a number of different synchronizing protocols that are fairly labor intensive, recommendations have been made to include reproduction vaccination (including IBR) as apart of these protocols. Naïve heifers were synchronized and vaccinated with MLV or inactivated vaccines 7 days prior to AI breeding. Following AI, a cleanup bull was added to the herd. The overall conception rate was 48% compared to 90% in the unvaccinated controls. The levels of estradiol, the hormone that is important for follicular development, where significantly lower in the naïve animals vaccinated with MLV. Heifers administered the MLV vaccine had a greater percentage of abnormal estrous cycles (38%; 8/21) when compared to the control group or a group given inactivated vaccine. Of the heifers that experienced an abnormal estrous cycle, 100% of heifers administered the inactivated vaccine (one or two dose) conceived at their return estrus; whereas, only 38% of heifers administered the MLV vaccine conceived in the subsequent estrus. During the synchronization period concentrations of estrogen were greater in both the controls and the two dose inactivated group when compared to the MLV group. Following AI, concentrations of progesterone were greater in control heifers compared to both the inactivated and MLV groups, but were similar between the inactivated and MLV groups. This data shows that naïve heifers vaccinated with the inactivated vaccine were less likely to have an abnormal estrous cycle and had statistically higher pregnancy rates when compared to the heifers vaccinated with the MLV vaccine. In summary, vaccination of naïve heifers with an MLV vaccine at the start of a fixed-time AI protocol can have a negative effect on pregnancy success. The recommendation would be to use MLV vaccine in the heifer development program and then follow up with inactivated vaccines at synchronization time. If MLV are used at synchronization time, it is really important that MLV be used in heifers that have developed a good immune response from a heifer vaccination program. Remember just because heifers have been “well vaccinated” does not mean they have developed a good immune response

Vaccination and Colostrum

Colostrum formation. The lack of antibody transfer in the developing fetal calf makes the importance of colostrum ingestion paramount. Colostrum with high immunological activity is a product of proper vaccination and nutrition in the dam.

Colostrogenesis. Colostrum synthesis in the mammary gland of the pregnant female is dependent on two factors: the presence of serum antibodies and a transport mechanism to move the antibody, primarily immunoglobulin G1 (IgG1), into the mammary gland. Although the pregnant cow must be immunosuppressed to maintain the allergenic fetus (otherwise the bovine fetus would be rejected), this immunosuppression appears to occur most strongly in the uterus and the placenta. This fetal protective immunosuppression does not appear to cause a high level of generalized systemic immunosuppression that affects the cow's antibody response to vaccines or environmental antigens. However, some effect on the cell-mediated adaptive responses is observed in the pregnant animal. The movement of antibody from the circulation to the mammary gland is hormonally regulated and begins 2-3 weeks prior to calving and has its highest transport in the last 1-2 weeks of pregnancy. This coincides with increases in estrogen, decreases in progesterone and increase in the neonatal receptor (FcRn) in the mammary gland. This small window of colostrogenesis makes timing of vaccine administration to the dry cow important. Non-adjuvanted vaccines would need to be given within 4 weeks of calving to get maximum circulating levels during colostrogenesis. Adjuvanted vaccines could be given earlier in the dry cow period, as they sustain higher antibody levels for longer periods of times. This ability to concentrate antibody ends rapidly after parturition. Colostrum from cows with premature calves will have lower levels of antibodies, so premature calves should be fed colostrum from cows that delivered full term calves.

Colostrum components. Colostrum's immunological component is composed primarily of antibodies, cytokines and cells. Antibody is an extremely critical component of colostrum and provides an immediate source of antibody for the agammaglobulinemic calf. Colostrum contains 32-212 mg/ml of total IgG (20-200 mg/ml IgG1 and ~12 mg/ml IGg2). Calves that ingest colostrum shortly after birth have significant concentrations of immunoglobulin in serum, while colostrum deprived calves have only trace amounts of immunoglobulin during the first 3 days of life. Production of IgM in colostrum-deprived calves does not begin to appear in the circulation until four days after birth and doesn't reach functional levels (1 mg/ml) until eight days of age. Levels of circulating IgA, IgG_1, and IgG_2 do not reach appreciable levels in these calves until 16 to 32 days after birth. The levels of these antibodies do not approach adult levels until about four months after birth, at this time IgG_2 is only half of adult levels indicating a strong TH2 bias.

It has been well demonstrated that preparturient vaccination of the cow for enteric diseases such as colibacillosis, *Clostridial perfringens*, cryptosporidiosis, and rotaviruses results in production of pathogen-specific antibodies that provide protection for the neonate against severe disease. Similar protection is also seen against respiratory pathogens including infectious bovine rhinotracheitis (IBR-bovine herpesvirus 1), bovine respiratory syncytial virus (BRSV), and bovine viral diarrhea virus (BVDV). The quantity and the overall quality (i.e. not contaminated with bacteria and/or spoiled,

having a relatively high concentration of total protein and sufficient fat) are important. Keeping colostrum free of microbial contaminants makes good collection and storage imperative, particularly in operations that pool and feed "normalized" colostrum – a practice that has favor in dairy operations.

The second family of components of colostrum is cytokines. These immunological hormones help in the development of the fetal immune response. It is not clear if these cytokines are secreted in the mammary gland or produced by the leukocytes found in colostrum, or both. Interleukin 1-beta (IL-1beta), IL-6, tumor necrosis factor beta (TNF-beta) and interferon-gamma (INF-gamma) are present in bovine colostrum and are associated with a pro-inflammatory response and may help in the recruitment of neonatal lymphocytes into the gut to aid in normal immune development. Colostrum rapidly improves the ability of neutrophils to phagocytize bacteria, which is primarily accomplished by absorption of small molecules like cytokines. Work in pigs has demonstrated that colostral cytokines are absorbed and can be detected in the blood. The level of these cytokines (IL-4>IL-6>INF-gamma>IL-10) peaked at 1-2 days postpartum. The high levels of two anti-inflammatory cytokines IL-4 and transforming growth factor beta-1 (TGF-beta1) would suppress local secretion of pro-inflammatory cytokines in the intestine allowing gut microbial colonization.

The third family of components of colostrum is cells. Colostrum contains between $1x10^6$ and $3x10^6$ cells/ml and are almost exclusively leukocytes. These viable leukocytes are present in percentages similar to peripheral blood, but with a larger fraction of macrophages (40-50%) and a smaller fraction of lymphocytes (22 to 25%) and neutrophils (25 to 37%). The vast majority of lymphocytes are T-lymphocytes with less than 5% being B-lymphocytes. Some of these maternal cells enter the circulation and reach peak levels 24 hrs after birth. Animals that receive colostrum containing maternal leukocytes develop antigen presenting cells (APC) faster, which is important since APCs are the keystone cell for the development of an acquired immune response to pathogens or vaccines. Additionally, pathogen specific maternal T lymphocytes from vaccinated cows have been isolated from the neonatal calf with maximum inducible proliferation at 1 day following birth. The exact role of these cells in the long-term development of pathogen specific acquired immunity is not clear as they are no longer detectable in the circulation at 7 days of age. The take home message is that colostrum has many important components again emphasizing the importance of good colostrum intake by the newborn calf. In addition the timing of vaccinating the pregnant cow for good colostrum immunity is important. Oil-adjuvanted scour products have the advantage of providing longer antibody levels that allows them to be given early during pregnancy

References

1) Van der Maaten MJ, Miller JM, Whetstone CA. Ovarian lesions induced in heifers by intravenous inoculation with modified-live infectious bovine rhinotracheitis virus on the day after breeding. 1985. Am J Vet Res 46:1996-9.
2) Perry GA, Zimmerman AD, Daly RF, et al. Effects of vaccination of naïve beef heifers on serum hormone concentrations and conception rates. Theriogenology, in press.

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