Vaccinating Calves: New Information on the Effects of Maternal Immunity

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Abstract

For decades, veterinarians have believed that young animals with circulating maternally-derived antibody cannot be effectively vaccinated. However, many investigators have shown that young animals vaccinated in the face of maternal antibody (IFOMA), while not showing evidence of an increase in serum antibody titer typically seen in older animals responding to vaccination, will show evidence of T cell activation or, better yet, protection from disease when they are exposed to infection after maternal antibodies have disappeared. Successful priming for a memory immune response by vaccination IFOMA has repeatedly been shown to be possible in calves. In general, successful vaccination of calves with moderate levels of maternal antibody requires two doses of modified-live vaccine given at least 2-4 weeks apart, but exceptions to this rule have been identified. While two doses are more likely to be successful, in some cases it has been possible to protect calves from disease months later by vaccination with a single dose of modified-live vaccine given intranasally or parenterally when they are within two months of age. However, these findings are not consistent; occasionally young animals vaccinated IFOMA fail to develop a protective immune response to later challenge. Reasons that calves are often but not always successfully protected when vaccinated IFOMA are not completely defined, but are likely related to age of the animal at vaccination, amount of maternal antibody present, type of vaccine the calf receives, virulence of the challenging pathogen, and the outcome used to define success of vaccination. While more research is needed before consistently reliable recommendations for successful vaccination of calves IFOMA can be made, ample evidence suggests that vaccination IFOMA can protect calves from disease when they are exposed to infectious agents after maternal antibodies have disappeared in at least some cases. Thus, vaccination IFOMA may be worthwhile and cost effective practice when young calves are at reasonably high risk of disease due to agents for which effective vaccines are available.

Résumé

Pendant plusieurs décennies, les vétérinaires ont cru que les jeunes animaux possédant un anticorps circulant d'origine maternelle ne pouvaient être vaccinés efficacement. Toutefois, de nombreux chercheurs ont démontré que les jeunes animaux vaccinés en présence d'anticorps d'origine maternelle (IFOMA, *in the face of maternal antibody*), bien que ne démontrant pas d'évidence d'une augmentation du titre de l'anticorps sérique qui est habituellement observée chez des animaux plus âgés en réaction à la vaccination, présenteront des signes d'activation des lymphocytes T ou, mieux encore, une protection contre la maladie lorsqu'ils seront exposés à une infection après la disparition des anticorps maternels. Il a été plusieurs fois démontré qu'il est possible d'induire une sensibilisation par primovaccination en vue d'obtenir une réponse mémoire chez des veaux IFOMA. En général, la vaccination des veaux qui présentent des niveaux moyens d'anticorps d'origine maternelle réussit avec deux doses de vaccin à virus vivant modifié administrées à intervalle d'au moins 2 à 4 semaines; il y a tout de même eu des exceptions à cette règle. Bien que le succès de la vaccination soit plus probable avec deux doses, dans la plupart des cas, il a été possible de protéger les veaux d'une maladie apparaissant plusieurs mois plus tard au moyen d'une seule dose de vaccin à virus vivant modifié administrée par voie intranasale ou parentérale avant l'âge de deux mois. Cependant, ces résultats ne sont pas cohérents, puisqu'il arrive occasionnellement que de jeunes animaux vaccinés IFOMA ne développent pas de réaction immunitaire protectrice contre une infection expérimentale ultérieure. Les raisons qui expliquent pourquoi les veaux sont souvent – mais pas toujours – protégés avec succès lorsqu'ils sont vaccinés IFOMA ne sont pas entièrement définies, mais elles sont probablement associées à l'âge de l'animal au moment de la vaccination, à la quantité d'anticorps d'origine maternelle présente, au type de vaccin reçu, à la virulence du pathogène de provocation, et au résultat utilisé pour définir le succès de la vaccination. Les recherches doivent évidemment se poursuivre avant que des recommandations toujours fiables sur une vaccination réussie de veaux IFOMA puissent être formulées; par ailleurs, de multiples éléments de preuve suggèrent, à tout le moins dans quelques cas, que la vaccination de veaux IFOMA peut protéger les veaux de la maladie lorsque ceux-ci sont exposés à des agents infectieux après la disparition des

anticorps maternels. La vaccination IFOMA peut donc représenter une pratique valable et rentable lorsque de jeunes veaux sont exposés à un risque de maladie passablement élevé lié à des agents pour lesquels il existe des vaccins efficaces.

Introduction

For decades, veterinarians have been taught that young animals with circulating maternally-derived antibody cannot be vaccinated while maternal antibodies persist. This understanding has been based on research and some clinical experience in animals and humans. Thus, vaccination schedules for young animals were aimed at timing vaccination to coincide with the time that maternal antibodies had disappeared, or administering multiple doses of vaccine at intervals though the neonatal period to "catch" the window of time when maternal antibody had waned, but before the young animal was infected with the agent of interest. However, many investigators have determined that young animals vaccinated in the face of maternal antibody (IFOMA) can indeed mount an immunologic response to vaccination, and that vaccination IFOMA can protect young individuals from infectious disease once maternal antibody titers have decreased to levels no longer protective. In fact, in a few cases, young animals vaccinated IFOMA have been shown to have superior responses to later challenge, as compared to young animals lacking maternal antibody and vaccinated at a comparable age;[5,22,25] these studies imply that maternally-derived immune factors may actually improve the response to vaccination in some cases. Although vaccination IFOMA is not always successful in priming a neonate to have a protective immune response to later challenge, it has been repeatedly shown to be possible to improve the immune response of calves vaccinated IFOMA, if certain factors are considered when vaccination strategies are planned. This article will review the literature on the subject of vaccination IFOMA, focusing on research studies in cattle, with a few references to studies in other species. Although many questions remain unanswered regarding the best way to effectively vaccinate calves IFOMA, research exists that provides for some evidence-based recommendations. Thus, suggestions based on currently available research for the clinical application of vaccination of calves IFOMA will be made.

Experimental Studies of Vaccination in the Face of Maternal Antibody (IFOMA)

Broadly, the effect of maternal antibody on the ability of calves to respond to vaccination has been evaluated in the laboratory setting in two major ways: 1) calves with circulating maternal antibodies are vaccinated, and researchers look for an increase in serum antibody (seroconversion) or evidence of T cell activation in cell culture weeks to months after vaccination; or 2) calves with circulating maternal antibodies are vaccinated, and researchers experimentally challenge calves with a virulent form of the infectious agent in the vaccine months later, when maternal antibodies have disappeared, and measure the ability of calves to mount a protective response against infection. Measuring seroconversion or T cell responsiveness in calves vaccinated IFOMA can provide evidence that the immune system has been primed to respond. However, studies where calves are actually infected are more meaningful, because protection of vaccinated calves against disease following challenge provides stronger evidence that vaccination IFOMA leads to a clinically significant immune response.

Studies of seroconversion or T cell responsiveness in calves vaccinated IFOMA

To a large degree, the commonly held understanding that vaccination IFOMA cannot stimulate an immune response came from research and clinical experience that showed that children and young animals vaccinated IFOMA would not display an increase in serum antibody two to four weeks after vaccination—that is, they would not seroconvert following vaccination.[1,9,11,27] Seroconversion, identified by a 4-fold or greater increase in the titer of serum antibodies against a specific infectious agent, is a standard measure of specific activation of the immune response. Therefore, lack of seroconversion in young individuals vaccinated IFOMA was presumed to mean that the immune system had not been stimulated by vaccination. However, some researchers recognized that, while young individuals might not seroconvert following initial vaccination, they would produce high levels of antibody consistent with a memory (anamnestic) response when vaccinated again after maternal antibodies waned. For example, calves receiving a dose of modified-live virus (MLV) infectious bovine rhinotracheitis virus (IBRV) vaccine between 2-3 months of age in the presence of high levels of maternally-derived serum neutralizing antibodies did not seroconvert, but when these calves received a second dose of vaccine at 7-8 months of age, they rapidly produced high levels of neutralizing antibody at a rate consistent with a memory response.[2] In a similar study, calves vaccinated with MLV IBRV at 2.5 months of age did not seroconvert following vaccination, but when vaccinated again at 6.5 months of age, they developed levels of serum neutralizing antibody that were significantly higher after one week than serum antibody levels in calves vaccinated for the first time at 6.5 months of age.[17]

Other evidence that vaccination IFOMA can induce an immune response in calves was identified by re-

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searchers who measured the decline of antibody titers in calves over several months' time following vaccination IFOMA, and compared the rate of decline to that in calves not vaccinated IFOMA. Kaeberle *et al*[14] evaluated the effect of three different commercially available killed virus multivalent vaccines (containing IBRV, bovine viral diarrhea virus [BVDV], bovine respiratory syncytial virus [BRSV] and parainfluenza type-3 virus [PI3]) on serum neutralizing antibody titers in calves vaccinated for the first time when they were 28-69 days old, and boosted 32 days later. In this study, calves that received one of the vaccines[a] had significantly higher serum neutralizing antibody levels to IBRV, BVDV type 1, BVDV type 2 and PI3 at three months after they received the second dose of vaccine than did calves in the other two vaccine groups, or calves that received no vaccination.[13] The fact that one killed virus vaccine was able to stimulate persistently elevated serum antibodies in calves vaccinated IFOMA, while two other killed virus products did not, implies that the formulation of the vaccine and/or the adjuvant contained in the vaccine may have been important in successfully stimulating persistently high antibody titers in calves vaccinated IFOMA. A similar study of the effect of vaccination IFOMA on the persistence of serum antibody levels was carried out by Hodgins and Shewen,[12] who showed that colostrum fed calves vaccinated at six and eight weeks of age with a *Mannheimia haemolytica* culture supernatant vaccine[b] had levels of agglutinating and leukotoxin neutralizing antibodies that were significantly higher at 10 weeks of age than those in calves not vaccinated. In this study, calves vaccinated at two and four weeks of age also had higher agglutination titers at 10 weeks of age than nonvaccinated calves, but leukotoxin neutralizing titers (which are particularly important in mediating protection against disease due to *M. haemolytica*) were not. These investigators concluded that administration of the vaccine used in the study could be effective when administered IFOMA to calves as young as six weeks of age, but protection in younger calves would not be as reliable.

In a field study of the effect of vaccination IFOMA on antibody persistence, calves vaccinated IFOMA at one and two months of age with a *M. haemolytica*/*Haemophilus somnus* vaccine[c] had significantly higher titers of serum antibodies to both bacteria at four and six months of age than did nonvaccinated herdmates.[25] In a separate trial, these investigators compared the effect of vaccinating calves with the *M. haemolytica*/*H. somnus* vaccine IFOMA at three and four months of age, or at four months of age only. Calves vaccinated twice had higher antibody titers to *H. somnus* at six months of age when compared to unvaccinated calves, but calves vaccinated only once did not have higher titers to either *M. haemolytica* or *H. somnus* at six months of age. In this trial, it appeared to be important for calves to receive two doses of vaccine in order to induce persistently elevated serum antibody levels at six months of age.

Fulton *et al*[10] also evaluated the effect of vaccination IFOMA on the duration of serum neutralizing antibody titers in a field setting. Calves receiving an inactivated IBRV/BVDV type 1/BVDV type 2/BRSV/PI3 vaccine[d] at branding (approximately two months of age) and again at weaning (approximately five months of age) had significantly higher neutralizing antibody titers to IBRV, BVDV type 1, BVDV type 2 and PI3 virus than nonvaccinated herdmates at the time of delivery to a feedlot, 21 days after the second vaccination.

Research has also evaluated the effect of vaccination IFOMA on T cell responses to agents in vaccines. Calves vaccinated at 10 days of age IFOMA with a MLV/IBRV/BRSV/PI3/inactivated BVDV vaccine[e] as well as a *M. haemolytica* bacterin-toxoid[f] had significantly higher lymphocyte blastogenesis responses to IBRV and BRSV 12 days after vaccination than nonvaccinated calves, indicating that T cells were activated to divide and expand in response to the vaccine.[6] Unlike the experiments described previously, calves in this study vaccinated IFOMA did not have higher titers of serum neutralizing antibody at weaning, and they did not produce higher serum neutralizing titers when they received booster vaccinations at weaning as compared to herdmates that were not vaccinated IFOMA at 10 days of age. The difference in antibody responses to vaccination IFOMA in this study as compared to others may have been related in part to the very young age at which calves received their first dose of vaccine IFOMA, or perhaps to the nature of the vaccine formulation administered.

In summary, the research described above showed by various measures that vaccines administered IFOMA can induce a measurable immune response in calves, and in most cases responses were significantly greater than those in control calves not vaccinated IFOMA.

Studies of resistance to disease following experimental challenge of calves vaccinated IFOMA

While *in vitro* or *ex vivo* measures of immune responsiveness have shown that calves vaccinated IFOMA can mount an immune response to vaccination, a more clinically relevant question is whether vaccination IFOMA can protect calves from disease due to infection later in the life of the calf, when maternal antibodies are no longer present. Calves vaccinated IFOMA with MLV BRSV by the intranasal route at three weeks of age were protected against BRSV challenge at three months of age, as measured by absence of viral shedding post-challenge.[15] Although numbers of calves in

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this study were small, results were notable in that shedding was not prevented in calves vaccinated IFOMA with killed BRSV administered intranasally, or MLV BRSV administered intramuscularly. This study suggested that efficacy of vaccination IFOMA can be related to the route of vaccination, as well as whether the vaccine is live or inactivated. Three more recent studies showed that calves vaccinated IFOMA with inactivated (killed) BRSV vaccines can be protected against challenge as measured by decreased viral shedding.[13,16,19] In two studies, calves that received two doses of inactivated or subunit BRSV vaccine within two months of age were protected against challenge 11-28 days after the second vaccination.[13,19] In the third study, calves received a single dose of killed BRSV/PI3/*M. haemolytica* vaccine IFOMA; while clinical disease was mild in both groups, vaccinated calves were significantly less likely to shed virus post-challenge than nonvaccinated control calves. In this study, calves that received a univalent MLV BRSV vaccine IFOMA did not shed less virus than controls following challenge.[16]

Some of the most complete and informative research on the value of vaccinating calves IFOMA has evaluated the effect of vaccinating very young calves to protect them against BVDV challenge. Three studies have used similar methods to undertake this effort. In the first,[7]neonatal calves were fed either colostrum with a high concentration of antibodies to BVDV or colostrum with no antibodies to BVDV. One group of calves with high colostrum-derived serum antibody titers to BVDV was vaccinated with a MLV multivalent BVDV type 1/IBRV/BRSV/PI3 vaccine[g] at 10-14 days of age, and a second group with no colostrum-derived serum antibodies to BVDV was also vaccinated at this time. A third group of calves had no colostrum-derived serum antibodies to BVDV, and was not vaccinated. A fourth group of calves with no colostrum-derived serum antibodies to BVDV was vaccinated at four months of age. All groups were challenged at 4.5 months of age with a virulent type 2 BVDV. Following challenge, all groups of calves had some signs of disease, but calves that had no serum antibodies to BVDV when vaccinated at 10-14 days of age, and calves that had no serum antibodies to BVDV and were vaccinated at four months of age, developed relatively mild disease. In contrast, calves vaccinated IFOMA (to BVDV), and calves that had no maternal antibody to BVDV and were never vaccinated, developed relatively severe disease that necessitated euthanasia of a majority of calves in each group. This study proved a few important points: 1) two-week-old calves vaccinated IFOMA with a MLV vaccine containing type I BVDV were not protected from relatively severe disease due to type 2 BVDV at 4.5 months of age; 2) calves with low to moderate levels of maternal antibody to BVDV were not protected from relatively severe type 2 BVDV induced-disease (although it should be noted that relatively high titers of maternal antibody can protect calves from type 2 BVDV challenge[4]); 3) very young (10-14 day old) calves with no colostrum-derived antibodies to BVDV could be safely and effectively vaccinated with a MLV vaccine containing type 1 BVDV, and these calves can be protected against severe disease following challenge four months later. It is important to note that the young "seronegative" calves vaccinated with the MLV vaccine were not completely seronegative in the sense that a colostrum-deprived calf would be, because they received colostrum that contained antibodies to pathogens other than BVDV, including (presumably) antibodies to the other viruses in the MLV vaccine. Thus, although the vaccine was safe in very young calves, they were not also seronegative to IBRV, which has been linked to disease in very young seronegative calves vaccinated with MLV IBRV vaccines.[3]

The second study examining the effect of exposure to BVDV IFOMA on protection against subsequent BVDV challenge evaluated calves that were not exactly vaccinated, but rather were exposed to (infected with) live type 2 BVDV by intranasal administration of live virus.[21] In this study, calves were either fed colostrum with high antibody titers to BVDV type 1 and type 2, or milk replacer. Thus, the calves in the "no colostrum" group were truly colostrum-deprived. When calves were infected with type 2 BVDV IFOMA at 2-5 weeks of age, they were protected from disease, while colostrum-deprived calves developed severe disease. Calves first exposed to the virus IFOMA at 2-5 weeks of age were exposed again at 7-9 months of age, after maternal antibody titers had decreased to less than 1:8. The responses of these calves to challenge at 7-9 months of age were compared to those of calves that received colostrum containing antibodies to BVDV, but had not yet been exposed to the virus, or calves that were colostrum deprived. Calves that had been infected IFOMA at 2-5 weeks of age were protected from disease at 7-9 months of age, even though they had little or no circulating antibody at the time of second challenge. In contrast, calves that had not been infected at 2-5 weeks of age, whether or not they initially received colostrum containing antibodies to BVDV, developed disease. This study proved a few important points: 1) infection of very young calves IFOMA could protect them from later re-infection with the same virus; and 2) this protection was present even though calves no longer had levels of serum antibody that would be considered protective. Thus, calves had been primed at 2-5 weeks of age for a protective immune response that kept them from developing disease at 7-9 months of age, and this protection was not mediated by serum antibodies present at the time of challenge. The investigators showed in a separate

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publication that the calves exposed at 2-5 weeks of age IFOMA had CD4, CD8 and gamma-delta T cells in their blood that responded to a significant degree to BVDV type 1 and type 2, as compared to calves not exposed at 2-5 weeks of age.[8] Moreover, these T cell responses were present at two weeks following the initial challenge, and persisted until the second challenge at 7-9 months of age. Therefore, calves infected IFOMA had developed T cells responsive to BVDV (although the calves did not seroconvert following infection IFOMA), and these T cells likely helped protect the calves from disease when they were infected again, after maternal antibodies waned.

In a third study investigating the effect of vaccination IFOMA on resistance to disease associated with BVDV infection, newborn calves were fed colostrum either with or without antibodies to BVDV.[28] At five weeks of age, calves from both groups were vaccinated with an adjuvanted MLV BVDV type 1 and type 2/IBRV/BRSV/PI3 vaccine[h]; a control group of calves that received colostrum without BVDV antibodies was not vaccinated. All calves were challenged with a virulent type 2 BVDV at 3.5 months after vaccination. Control calves that received colostrum without BVDV antibodies and were not vaccinated at five weeks of age developed evidence of severe disease, with significantly higher temperatures and clinical scores than calves in either vaccine group. There was no difference in the level of disease following challenge in either vaccinated group, indicating that calves without maternal antibody that were vaccinated at five weeks of age, and calves that were vaccinated IFOMA at 5 weeks of age were equally resistant to disease. Serum neutralizing antibody titers decreased in calves vaccinated IFOMA between the time of vaccination and challenge, while titers increased in calves without maternal antibody that were vaccinated, but the difference in serum neutralizing titers at vaccination was apparently not significantly different. Because a group of calves fed colostrum with antibodies to BVDV and not vaccinated was not included in this study, it was therefore not possible to separate the protective effect of maternal antibody from any protective effect of vaccination in this study. However, the study did show that administration of MLV multivalent vaccine could be safe in relatively young calves, even those lacking maternal antibodies to BVDV. In contrast to some studies where serum neutralizing titers stayed elevated over time in calves vaccinated IFOMA,[10,14,25] calves vaccinated IFOMA in this study had decreasing titers, and their titers did not increase in what appeared to be an anamnestic fashion after challenge.

In addition to the research described above, evidence also exists that calves can be protected from virulent challenge with *Leptospira* by vaccination IFOMA at four weeks of age[18] and from challenge with *Taenia saginata* in calves vaccinated IFOMA at 8-10 weeks of age.[20]

Field Trials of Vaccination IFOMA

Well-designed field trials in animals managed under standard husbandry practices are the best way to evaluate any vaccine or therapy. However, it is expensive, time consuming and logistically difficult to run well-designed field trials, and if naturally-occurring disease does not occur during a field trial, it may not be possible to determine if the vaccine or therapy in question had any beneficial effect. Therefore, it is unfortunate but not surprising that at this time there are relatively few published field trials testing the effect of vaccination of calves IFOMA on the occurrence of naturally-acquired disease. One commendable effort described the effect of vaccination of beef calves IFOMA in a herd with a history of unusually high incidence of pneumonia in nursing calves; BRSV and *M. haemolytica* had been isolated at necropsy of affected calves.[24] In the year following a period of high incidence of calf pneumonia, calves in the herd were vaccinated at three and five weeks of age with a MLV BRSV vaccine[i], a *M. haemolytica* leukotoxin/*H. somnus* bacterial extract vaccine,[c] or both vaccines; a fourth group of calves was left as an unvaccinated control group. Maternal antibody titers to BRSV, *M. haemolytica* leukotoxin and *H. somnus* were present in all calves. From the time between vaccination and weaning, the risk of treatment for respiratory disease, as deemed necessary by the producer, was lower in calves that received both vaccines (15% treated) as compared to calves that were not vaccinated (34% treated), although this difference was not statistically significant ($p = 0.13$). The relatively small number of calves in each group (26-29 calves per group) may have contributed to lack of statistical significance in this study. Mixing of vaccinated and nonvaccinated calves may have also impacted outcome; in vaccine trials where vaccinates are housed with nonvaccinated animals, herd immunity can protect nonvaccinates and bias the results toward no significant difference.

In a large trial of BVDV vaccination IFOMA in dairy calves at a calf rearing operation,[23] calves were vaccinated at 15 days of age with a multivalent vaccine containing killed BVDV,[j] and at 45 days of age with a multivalent vaccine containing live BVDV.[k] At the time of this study, both vaccines contained only type 1 BVDV. As measured by seroconversion, infection with type 1 BVDV was decreased in vaccinated calves within 60 days following vaccination. There was no significant difference in serum antibody titers between vaccinated and nonvaccinated calves at the time of first vaccination, so the protective effect associated with vaccination was not due to maternal antibody. There was no difference in

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crude morbidity (two or more treatments given on consecutive days as deemed necessary by farm staff) or mortality between vaccinated and nonvaccinated calves. Although the use of seroconversion as a measure of BVDV infection in this study had weaknesses outlined by the authors, the findings could be interpreted to mean that vaccination IFOMA could impact transmission of BVDV among young calves and possibly decrease the risk for disease.

Clinical Recommendations Based on Currently Available Research

As can be seen from the above literature review, the exact immunologic outcome in calves vaccinated IFOMA can vary, and this variation likely depends on many factors. These factors are not well characterized, but likely include the nature of the vaccine administered, number of doses administered, age of the calf and level of maternal antibody present in the calf, and the means by which a protective response is defined. However, in spite of these limitations, some recommendations can rationally be made:

1) Vaccination IFOMA of calves as young as one month of age can be successful in priming them for a protective immune response to viral respiratory pathogens at later challenge, even if challenge occurs when maternal antibodies have disappeared. MLV vaccines for the major viral respiratory pathogens (IBRV, BVDV type 1 and type 2, and BRSV) have most often been used in studies showing evidence of protection.

2) While a single dose of MLV viral vaccine given IFOMA to calves as young as one month of age can protect them from later disease, administration of two doses at 2 to 4 week intervals is preferable.

3) Vaccination of calves IFOMA at less than one month of age has not been as reliably protective as vaccination of calves greater than one month of age. If vaccination IFOMA of calves less than one month of age is undertaken, administration of a booster 2 to 4 weeks later is particularly recommended.

4) When calves are vaccinated IFOMA, antibody titers will typically not increase following vaccination. Thus, failure to seroconvert should not be interpreted as evidence of vaccination failure. Although seroconversion does not occur, T cells of calves vaccinated IFOMA can be found to be activated within days of vaccination, and increased T cell responsiveness may persist for weeks to months after vaccination IFOMA. Because assays measuring virus-specific or bacterial-specific T cell responses are not available in most diagnostic laboratories, it will likely not be practically possible to confirm the occurrence of specific T cell activation in calves vaccinated IFOMA in field settings.

5) If calves are suspected to have incomplete passive transfer or failure of passive transfer, studies have confirmed the safety and efficacy of a single dose of some currently available MLV vaccines for common respiratory viruses (BVDV type 1 and 2, IBRV, BRSV, and PI3) in seronegative calves under one month of age. Vaccination can sometimes protect very young seronegative calves from disease within days of vaccination, and the protection can last for months. However, it must be remembered that MLV vaccines have the potential to cause disease in significantly immunocompromised hosts, so the use of these products requires the veterinarian to judge each situation independently. Vaccination of sickly or malnourished calves with failure of passive transfer may be more safely undertaken the first time with a killed product, with a live product being given at a later date to provide a more broad and long-lasting immune response.

6) Although most studies of vaccination IFOMA have evaluated MLV viral vaccines, killed viral vaccines can sometimes prime calves effectively IFOMA. The success of a killed product in this regard is likely related to the specific formulation, including the adjuvant contained in the vaccine. Thus, evidence that one particular killed virus vaccine can be effective in priming calves for a protective immune response IFOMA should not be extrapolated to other killed virus vaccines.

Conclusions

Current research confirms that calves can often be primed to develop a protective immune response to later challenge when vaccinated for the first time IFOMA. Vaccination IFOMA induces activation of pathogen-specific T cells, and this activation occurs in the absence of seroconversion following the first vaccination. Protection of calves vaccinated IFOMA has been shown by *in vitro* and *ex vivo* assays of immune function, experimental challenge of vaccinated calves, and, in a small number of cases, by field trials indicating

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decreased rates of naturally-occurring disease or infection in calves vaccinated IFOMA. While more research is needed before perfect recommendations for successful vaccination of calves IFOMA can be made, evidence indicates that vaccination IFOMA can protect calves from disease when they are exposed to infectious agents after maternal antibodies have disappeared in at least some cases. Thus, vaccination IFOMA may be a worthwhile and cost-effective practice when nursing or postweaning calves are at reasonably high risk of disease due to agents for which effective vaccines are available. More studies of the value of vaccination IFOMA in field settings are needed to confirm the promising findings of laboratory studies of this practice.

Endnotes

[a]Vira Shield 5, Grand Laboratories Inc., Larchwood IA (now sold by Novartis Animal Health US Inc., Larchwood IA).

[b]Presponse, Langford Inc., Guelph ONT (now sold by Fort Dodge Animal Health, Fort Dodge IA).

[c]Somnu-Star Ph, Biostar Inc., Saskatoon SK (now sold by Novartis Animal Health, Mississauga ONT).

[d]Triangle 4+type II BVD, Fort Dodge Animal Health, Fort Dodge IA.

[e]Cattlemaster 4, SmithKline Beecham Animal Health, Exton, PA (now sold by Pfizer Animal Health, New York NY).

[f]OneShot, SmithKline Beecham Animal Health, Exton, PA (now sold by Pfizer Animal Health, New York NY).

[g]Resvac 4, Pfizer Animal Health, New York NY.

[h]Pyramid 5, Fort Dodge Animal Health, Fort Dodge IA.

[i]BRSV Vac, Bayvet, Etobicoke ONT.

[j]CattleMaster, Pfizer Animal Health, New York NY.

[k]Bovi-Shield 4, Pfizer Animal Health, New York NY.

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