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Immunologic Responses of Beef Calves to Concurrent Application of Modified-Live Viral Vaccine (Intranasal and Systemic Administration) and Systemically Administered *Mannheimia haemolytica* Bacterin-Leukotoxoid

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Abstract

A study was conducted to assess the immunological response to a *Mannheimia haemolytica* bacterin-leukotoxoid, given separately or concurrently with a multivalent intranasally administered modified-live viral vaccine to range beef calves. Initially 202 spring-born calves were screened for infectious bovine rhinotracheitis (IBR), bovine respiratory syncytial virus (BRSV), and *M. haemolytica* leukotoxin antibody titers on day -30. A total of 154 calves with day 0 geometric mean IBR titers of <1:6 were accepted into the study. Fifty-one calves were assigned to treatment group T1 (*M. haemolytica* bacterin-leukotoxoid only; One Shot®, Pfizer Animal Health, New York, NY) and 51 calves were assigned to group T2 (intranasal modified-live virus (MLV) bovine herpesvirus-1 (BHV-1) and parainfluenza-3 (PI3) vaccine; TSV-2®, Pfizer Animal Health) and *M. haemolytica* bacterin-leukotoxoid (One Shot®). Fifty-two calves were assigned to group T3 (intranasal MLV BHV-1, PI3, and BRSV vaccine (INFORCE™ 3, Pfizer Animal Health) and *M. haemolytica* bacterin-leukotoxoid (One Shot®). On day 0, all study calves were administered their assigned vaccine. On day 91, all calves in the study were administered a pentavalent MLV vaccine containing BHV-1, BVD types 1 and 2, BRSV, and PI3 antigens (Bovi-Shield GOLD® 5, Pfizer Animal Health) and *M. haemolytica* bacterin-leukotoxoid (One Shot®) at separate injection sites. On days 0, 14, 28, 91, and 112, blood samples were collected, serum separated, and held frozen until completion of the study, at which time samples were evaluated for IBR and BRSV serum neutralization antibody titers and *M. haemolytica* leukotoxin antibody concentrations. Results demonstrated concurrent administration of the intranasal vaccines and the *M. haemolytica* bacterin-leukotoxoid did not affect the bacterin-leukotoxoid serological response. Calves vaccinated with intranasal BRSV vaccine had a significant ($P<0.05$) increase in BRSV antibody response when revaccinated systemically with injectable 5-way MLV vaccine 90 days later. Vaccination with *M. haemolytica* bacterin-leukotoxoid at approximately eight weeks of age resulted in a statistically significant ($P<0.05$) anamnestic response following revaccination 90 days later.

Keywords: beef calves, virus vaccine, intranasal vaccine, *Mannheimia haemolytica*, leukotoxoid, immune response

Résumé

Une étude a été menée afin d'établir la réponse immunologique à une bactérine-leucotoxine de *Mannheimia haemolytica* donnée séparément ou conjointement avec un vaccin multivalent à virus vivants modifiés administré par voie nasale chez des veaux de boucherie au pâturage. Parmi 202 veaux du printemps soumis au dépistage de la rhinotrachéite infectieuse bovine (IBR), du virus respiratoire syncytial bovin (BRSV) ou de titres d'anticorps anti-leucotoxine de *Mannheimia haemolytica* au jour 30, un total de 154 veaux avec une moyenne géométrique des moindres carrés des titres de moins de

1:6 au jour 0 ont été inclus dans l'étude. Un total de 51 veaux ont été alloués soit dans le groupe T1 (la bactérine-leucotoxine de *Mannheimia haemolytica* seulement, One Shot®, Pfizer Animal Health, New York, NY) ou soit dans le groupe T2 (vaccin à virus vivants modifiés administré par voie nasale et contenant l'herpèsvirus bovin 1 et le virus parainfluenza 3, TSV-2®, Pfizer Animal Health, avec la bactérine-leucotoxine de *Mannheimia haemolytica*, One Shot®). Un total de 52 veaux ont été alloués dans le groupe T3 (vaccin à virus vivants modifiés administré par voie nasale et contenant l'herpèsvirus bovin 1, le virus parainfluenza 3, le virus respiratoire syncytial bovin, INFORCE™ 3, Pfizer Animal Health, de même que la bactérine-leucotoxine de *Mannheimia haemolytica,* One Shot®). Au jour 0, tous les veaux ont été traités avec leurs produits de traitements désignés. Après 91 jours suivant le traitement initial, tous les veaux de l'étude ont reçu des injections sous-cutanées d'un vaccin pentavalent à virus vivants modifiés (virus de la diarrhée virale bovine du type 1 et 2, l'herpèsvirus bovin du type 1, virus parainfluenza du type 3 et le virus respiratoire syncytial bovin, Bovi-Shield GOLD® 5, Pfizer Animal Health) et de la bactérine-leucotoxine de *Mannheimia haemolytica* (One Shot®) a un autre site d'injection. Des échantillons de sang ont été recueillis aux jours 0, 14, 28, 91 et 112 et le sérum a été séparé et congelé jusqu'à la fin de l'étude. À ce moment, les titres de neutralisation sérique contre IBR et BRSV et la concentration d'anticorps anti- leucotoxine de *Mannheimia haemolytica* ont été établis avec les échantillons. Les résultats démontrent que l'administration conjointe du vaccin par voie nasale et de la bactérine-leucotoxine de *Mannheimia haemolytica* n'a pas eu d'impact négatif sur la réponse sérologique à la bactérine-leucotoxine. Les veaux vaccinés avec le vaccin BRSV par voie nasale montraient un accroissement statistiquement significatif ($P<0.05$) de la production d'anticorps contre le BRSV lorsque revaccinés systématiquement avec le vaccin pentavalent à virus vivants modifiés 90 jours plus tard. La vaccination avec la bactérine-leucotoxine de *Mannheimia haemolytica* lorsque les veaux étaient âgés approximativement de huit semaines entraina une réponse anamnestique statistiquement significative ($P<0.05$) suivant la revaccination 90 jours plus tard.

Introduction

During the past five decades, food animal veterinarians have developed vaccination protocols for cattle producing clients that not only help provide protection against diseases afforded by vaccines and bacterins, but were needed based on disease history and risk factors present in individual herds. Protocols were developed in a fashion consistent with conventional processing events of beef herds, such as branding and weaning. These efforts led to concurrent administration of multiple vaccines and bacterins, and little information is available regarding safety or efficacy of concurrent product administration. As early as 1991, information was published on immunologic interference of one viral antigen with a different, concurrently administered viral antigen.[18] The potential for immunologic interference between cattle concurrently administered modified-live virus (MLV) bovine herpesvirus-1 (BHV-1) vaccine and a *Mannheimia haemolytica* bacterin-leukotoxoid was first published in 1992.[9] Results suggested viral antigen interference with the immunologic response to a bacterial antigen when given concurrently.[9] Several studies have reported similar findings.[4,6,14,15,19]

Objectives of the field study reported here were to: 1) assess the immunological response to a *M. haemolytica* bacterin-leukotoxoid, given separately or concurrently with either a MLV intranasal (IN) BHV-1, bovine respiratory syncytial virus (BRSV), and parainfluenza-3 (PI3) vaccine or a MLV IN BHV-1 and PI3 vaccine in nursing range beef calves; 2) evaluate the effect of concurrent IN administration of BHV-1 (also called infectious bovine rhinotracheitis virus or IBRV) and subcutaneous administration of a *M. haemolytica* bacterin-leukotoxoid on the immunologic response when *M. haemolytica* bacterin-toxoid is administered concurrently with a pentavalent MLV vaccine on day 91; and 3) evaluate the effect of IN BRSV vaccine on the serological response when BRSV vaccine is administered by injection on day 91.

Materials and Methods

Study Facility

The study was conducted at the North Central Grasslands Research Extension Center, Streeter, North Dakota, a university extension research livestock operation in south-central North Dakota. Native grass pastures were utilized and water was provided via wells or sloughs. Pastures did not have holding corrals, alleyways or chute facilities; therefore, cattle were trailed to the main ranch facility for each processing. The mature crossbred cows used in this study, ranging in age from three to 10 years, were predominantly Angus-based. All cows had received a multivalent MLV vaccine containing BHV-1, bovine viral diarrhea virus (BVDV) types 1 and 2, and PI3 antigens that also included *Campylobacter fetus* and five serovars of leptospira[a] prior to the previous breeding season (spring 2009), and approximately 30 days prior to screening the calves for trial inclusion.

Animals

Calves in the study were born in the spring of 2010 on the ranch, and were selected on the basis of day -30 BHV-1 antibody titers. Only calves determined to have low BHV-1 titers, defined as a BHV-1 serum neutral-

izing (SN) antibody level of 1:6 or less, were included in the study. One-hundred fifty-four calves ranging in age from 10 to 13 weeks on day 0 qualified for the study and were randomly assigned to one of three treatment groups. On day 0, each calf was treated following the described protocol and a blood sample was collected. Following the day 91 processing, calves were weaned and placed in dry-lot until the final processing. Each calf was administered duplicate ear tags for purposes of identification. No calves were excluded from the data base, and data were collected for all calves on each day of the trial specified in the protocol.

Study Groups

A total of 202 spring-born calves native to the study ranch were screened for existing IBRV and BRSV titers, and *M. haemolytica* leukotoxin antibody concentrations 30 days prior to the initiation of the study. One-hundred fifty-four calves with day 0 SN IBR titers of <1:6 were enrolled in the study. Calves were blocked by day -30 leukotoxin titer, randomized to one of three treatment groups using a random number generator, and commingled on native pasture throughout the study.

Fifty-one calves were assigned to treatment group one (T1 – *M. haemolytica* bacterin-leukotoxoid[b] only), and 51 were assigned to treatment group two (T2 – MLV intranasal (IN) BHV-1 and PI3 vaccine[c] and *M. haemolytica* bacterin-leukotoxoid[b]). Fifty-two calves were assigned to treatment group three (T3 – MLV IN BHV-1, PI3, and BRSV vaccine[d] and *M. haemolytica* bacterin-leukotoxoid[b]). On day 0, when approximately 11 weeks of age, calves allotted to the study were administered vaccine(s) specified in the protocol and blood samples were collected. Multiple serials of products were used when more than one serial was commercially available to reduce the possible impact of serial variation. Three serials of *M. haemolytica* bacterin-leukotoxoid[b], two serials of MLV IN BHV-1 and PI3 vaccine[c], and one serial of IN BHV-1, PI3, and BRSV vaccine[d] were used. Each treatment group received an equal number of doses of each serial.

On day 91, all calves in each treatment group were given subcutaneous (SC) injections of a pentavalent MLV vaccine (BHV-1, BVDV types 1 and 2, PI3, and BRSV[e]) and *M. haemolytica* bacterin-leukotoxoid[b] on opposite sides of the neck. Two different lots of each product were used, with each treatment group receiving an equal number of doses of each lot. Additionally, all calves in each treatment group were administered a SC injection of a 7-way clostridial bacterin-toxoid/*Histophilus somni* bacterin[f] and a topical endectocide[g] at weaning.

Sample Collection and Analysis

On study days 0, 14, 28, 91, and 112, blood was collected (10 mL) from all calves and transported to the North Dakota State University Veterinary Diagnostic Laboratory, where serum was separated and held frozen at -4°F (-20°C) until completion of the study. Serums were analyzed after completion of the study for leukotoxin neutralizing antibody concentration by the Department of Veterinary Pathobiology at Oklahoma State University, and for IBR and BRSV SN antibody titers by the Oklahoma Animal Disease Diagnostic Laboratory by procedures previously reported.[6]

Statistical Methods

All data were recorded using specifically designed forms supplied by Pfizer Animal Health. Data and laboratory results were analyzed by the sponsors of the study.[h]

Serum antibody titers were transformed to the log scale and analyzed with a linear mixed model with repeated measures that included the fixed effects of treatment, day of study, and the interaction, along with the random effects of replicate (block). Day -30 antibody titers were included as a covariate in the analysis of all antibody titer results. Least square mean estimates of antibody titers from day 0 to 112 were generated and back-transformed to geometric means for presentation. Denominator degrees of freedom were calculated using the Kenward-Roger method within PROC MIXED of SAS.[i]

A significant ($P \leq 0.05$) treatment or treatment by day of study interaction was required before conducting pairwise tests of treatment differences.

Results

All 154 calves were present at all processing times for administration of test vaccines and blood sample collection; all calves completed the study. No significant differences ($P<0.05$) were found in the percent of calves that responded, or magnitude of the response, to *M. haemolytica* bacterin-leukotoxoid[b] administered at day 0 or day 91 in any of the treatment groups. When compared to previous studies,[6] where concurrent administration of a multivalent SC viral vaccine and SC administered *M. haemolytica* bacterin-leukotoxoid reduced the serological response to the bacterin-leukotoxoid, concurrent administration of multivalent IN viral vaccines and SC administered *M. haemolytica* bacterin-leukotoxoid resulted in the same serological response to the bacterin-leukotoxoid as when the toxoid was administered independently, as measured by humoral antibody concentration. There was a significant ($P<0.05$) anamnestic serologic antibody response to the *M. haemolytica* bacterin-leukotoxoid[b] administered at day 91 when compared to the magnitude of response seen following initial vaccination on day 0. The initial serologic antibody response against leukotoxin was seen as early as day 14 post-vaccination.

No significant differences in day 0 BRSV or IBR SN titers were found between groups (Tables 1 and 2). There was evidence of BRSV infection in adult beef cattle

Table 1. Least Squares Geometric Means of BRSV neutralizing antibody at days 0, 28, 91, and 112.

Treatment†	Day 0 titer	Day 28 titer	Day 91 titer	Day 112 titer
T1	7.96[a*]	5.46[a]	2.59[a]	4.31[a]
T2	8.15[a]	5.36[a]	2.26[a]	3.99[a]
T3	8.24[a]	5.97[a]	2.53[a]	9.62[b]

†T1 calves were vaccinated on day 0 with *Mannheimia haemolytica* bacterin-leukotoxoid (One Shot®, Pfizer Animal Health, New York, NY); T2 calves were vaccinated on day 0 with *M. haemolytica* bacterin-toxoid (One Shot®) and intranasal IBR-PI3 vaccine (TSV-2®, Pfizer Animal Health); T3 calves were vaccinated on day 0 with *M. haemolytica* bacterin-toxoid (One Shot®) and intranasal IBR, PI3, and BRSV vaccine (INFORCE™ 3, Pfizer Animal Health). All calves were vaccinated subcutaneously on day 91 (weaning) with a pentavalent MLV IBR, BVD (types 1 and 2), PI3, BRSV vaccine (Bovi-Shield GOLD® 5, Pfizer Animal Health), *M. haemolytica* bacterin-leukotoxoid (One Shot®), and 7-way clostridial bacterin-toxoid with *Histophilus somni* (Ultrabac® 7/Sombac®, Pfizer Animal Health).

*Values in a column with different superscripts are statistically significantly different at $P \leq 0.05$

Table 2. Least Squares Geometric Means of BHV-1 neutralizing antibody at days 0, 28, 91, and 112.

Treatment†	Day 0 titer	Day 28 titer	Day 91 titer	Day 112 titer
T1	4.52[a*]	2.89[a]	2.03[a]	2.14[a]
T2	5.17[a]	3.17[a]	2.05[a]	2.17[a]
T3	4.52[a]	2.91[a]	2.03[a]	2.06[a]

†T1 calves were vaccinated on day 0 with *Mannheimia haemolytica* bacterin-leukotoxoid (One Shot®, Pfizer Animal Health, New York, NY); T2 calves were vaccinated on day 0 with *M. haemolytica* bacterin-toxoid (One Shot®) and intranasal IBR-PI3 vaccine (TSV-2®, Pfizer Animal Health); T3 calves were vaccinated on day 0 with *M. haemolytica* bacterin-toxoid (One Shot®) and intranasal IBR, PI3, and BRSV vaccine (INFORCE™ 3, Pfizer Animal Health). All calves were vaccinated subcutaneously on day 91 (weaning) with a pentavalent MLV IBR, BVD (types 1 and 2), PI3, BRSV vaccine (Bovi-Shield GOLD® 5, Pfizer Animal Health), *M. haemolytica* bacterin-leukotoxoid (One Shot®), and 7-way clostridial bacterin-toxoid with *Histophilus somni* (Ultrabac® 7/Sombac®, Pfizer Animal Health).

*Values in a column with different superscripts are statistically significantly different at $P \leq 0.05$

in the herd, based on calf antibodies (Table 1) assumed to be maternally-derived and a history documenting no BRSV vaccine had been administered to any of the cows. Following day 0 sampling and administration of a MLV BRSV-containing IN vaccine[d] to calves with BRSV maternal antibody present, BRSV antibody titers continued to decline. There were no statistical differences between groups until day 112, when all groups had a significant ($P<0.05$) increase in BRSV titers following vaccination with a pentavalent MLV (BHV-1, BVDV types 1 and 2, PI3, and BRSV[e]) vaccine on day 91 of the study. A greater increase ($P<0.05$) was seen on day 112 in the BRSV antibody levels in group T3, which had been administered MLV IN BHV-1, PI3, and BRSV vaccine[d] on day 0, as compared to calves in groups T1 and T2.

Discussion

Because calves in the three treatment groups were commingled throughout the study, there could be concern that IN products could have shed BHV-1 to other treatment groups, thereby nullifying the *M. haemolytica* bacterin-leukotoxoid antibody concentration outcome comparisons. The authors believe this was unlikely because the calves were widely dispersed on pasture. In addition, only calves in group T3 had a significant anamnestic response to BRSV vaccine following parenteral vaccination with 5-way viral vaccine on day 91. Calves in groups T1 and T2 were not vaccinated with BRSV vaccine on day 0, and did not have an anamnestic response to vaccination with a MLV 5-way viral vaccine on day 91, further suggesting there was no viral shedding of intranasal vaccine between treatment groups.

In the current study, calves in group T1 were vaccinated only with *M. haemolytica* bacterin-leukotoxoid on day 0, and about 65% responded serologically. *M. haemolytica* titers from 2006 and 2008 studies[6] indicate that control calves in the 2006 study had a response rate similar to T1 calves in the current study; however, only 46% of older calves in the 2008 study responded serologically.

In the 2006 and 2008 studies, calves vaccinated concurrently with *M. haemolytica* and 5-way MLV vaccine had a reduction in response to the bacterin-leukotoxoid of about 15 percentage points. Results further suggest the that treatment groups T2 and T3, which received concurrent bacterin and MLV vaccine on day 0 in the current study, had similar response rates to the control calves in both the 2006 and 2010 studies, suggesting limited if any interference by BHV-1 or IBRV (Table 3).

When adjusted for similar day 0 starting levels, the magnitude of change in *M. haemolytica* antibody concentrations observed in the control group (T1) between day 1 and day 14 in the current study was very consistent with those observed in the control groups in the 2006 and 2008 studies,[6] where only injectable or systemic vaccines were used (Figure 1).

However, even if nasal shedding of BHV-1 had occurred among treatment groups, there is no evidence that concurrent administration of IN MLV vaccine had any negative immunologic effect on *M. haemolytica* antibody concentration, as calves concurrently administered IN viral vaccine and *M. haemolytica* bacterin-leukotoxoid had a 20 percentage-point swing (-15% to +5%) compared to calves vaccinated with injectable vaccines (Table 3).

Response to Mannheimia haemolytica Bacterin

The possibility of immunologic interference when cattle are concurrently administered a MLV BHV-1 vaccine and *M. haemolytica* bacterin-leukotoxoid was first published in 1992,[10] where investigators demonstrated that vaccination of feedlot calves with MLV BHV-1 vaccine decreased the serological response to an experimental *M. haemolytica* vaccine. This has since been demonstrated in multiple studies, both field-based[6,19] and in experimental models.[4,14,15] A decrease in *M. haemolytica* antibody levels was also demonstrated when a temperature-sensitive (TS) BHV-1 vaccine was administered systemically at the same time, although the decrease in response was less than seen when other MLV BHV-1 vaccines were given.[6]

The present study demonstrated that concurrent administration of MLV IN IBR-PI3 or IBR, PI3, and BRSV vaccine and *M. haemolytica* bacterin-leukotoxoid resulted in similar humoral antibody responses to the bacterin as when administered independently. Also, there was no difference in the effect of the two intranasal MLV vaccines on the immune response to the bacterin when administered independently (Table 4). The increase in *M. haemolytica* leukotoxoid antibodies over day 0 baseline levels when measured at days 14 and 28 was similar within each treatment group (Table 5). This further demonstrates that concurrent use of IN virus vaccines did not impair the immunologic response to *M. haemolytica* vaccination.

It is important to note that the MLV IN vaccines contained the TS BHV-1 variant. Interference could still be seen if a conventional MLV BHV-1 intranasal vaccine was co-administered with a *M. haemolytica* bacterin-leukotoxoid. The antibody response ($P<0.05$) seen at day 112 following the second administration of

Table 3. Percent of animals that responded with a two-fold or greater increase to day 0 *Mannheimia haemolytica* antibody concentrations.

	Bacterin only[a]	Bacterin + viral[b]	Difference
2006	61%	48%	-13% points
2008	46%	28%	-18% points
2010	67%	72%	+ 5% points

[a]*M. haemolytica*

[b]IBR, BVD (types 1 and 2), PI3, BRSV

Data from 2006 and 2008 studies adapted from Cortese VS, Seeger JT, Stokka GS, Hunsaker BD, Lardy GP, Weigel DJ, Brumbaugh GW: Serological response to *Mannheimia haemolytica* in calves concurrently administered inactivated or modified live preparations of *M. haemolytica* and viral combination vaccines containing modified live bovine herpesvirus type 1. Accepted for publication, *Am J Vet Res* 2011.

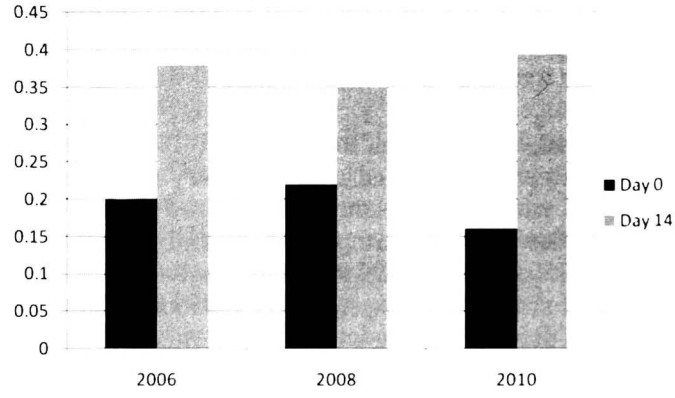

Figure 1. Antibody concentrations (nanograms/mL) for calves receiving only *Mannheimia haemolytica* bacterin-leukotoxoid in three independent studies. Data from 2006 and 2008 studies adapted from Cortese VS, Seeger JT, Stokka GS, Hunsaker BD, Lardy GP, Weigel DJ, Brumbaugh GW: Serological response to *Mannheimia haemolytica* in calves concurrently administered inactivated or modified live preparations of *M. haemolytica* and viral combination vaccines containing modified live bovine herpesvirus type 1. Accepted for publication, *Am J Vet Res* 2011.

Table 4. Least Squares Geometric Means of *Mannheimia haemolytica* leukotoxin neutralizing antibody at days 0, 14, 28, 91, and 112.

Treatment†	Day 0 titer (ng/mL)	Day 14 titer (ng/mL)	Day 28 titer (ng/mL)	Day 91 titer (ng/mL)	Day 112 titer (ng/mL)
T1	0.16[a*]	0.45[a]	0.34[a]	0.49[a]	0.95[a]
T2	0.14[a]	0.41[a]	0.32[a]	0.44[a,b]	0.99[a]
T3	0.15[a]	0.41[a]	0.33[a]	0.39[b]	1.00[a]

†T1 calves were vaccinated on day 0 with *Mannheimia haemolytica* bacterin-leukotoxoid (One Shot®, Pfizer Animal Health, New York, NY); T2 calves were vaccinated on day 0 with *M. haemolytica* bacterin-toxoid (One Shot®) and intranasal IBR-PI3 vaccine (TSV-2®, Pfizer Animal Health); T3 calves were vaccinated on day 0 with *M. haemolytica* bacterin-toxoid (One Shot®) and intranasal IBR, PI3, and BRSV vaccine (INFORCE™ 3, Pfizer Animal Health). All calves were vaccinated subcutaneously on day 91 (weaning) with a pentavalent MLV IBR, BVD (types 1 and 2), PI3, BRSV vaccine (Bovi-Shield GOLD® 5, Pfizer Animal Health), *M. haemolytica* bacterin-leukotoxoid (One Shot®), and 7-way clostridial bacterin-toxoid with *Histophilus somni* (Ultrabac® 7/Sombac®, Pfizer Animal Health).

*Values in a column with different superscripts are statistically significantly different at $P \leq 0.05$

**Overall test of treatment by day, P-value was 0.70

Table 5. Percent of animals within a treatment group that responded with "X" times the day 0 baseline levels of *Mannheimia haemolytica* leukotoxoid antibodies on days 14 and 28.

Treatment	≤ 1X		>1X & <2X		≥ 2X		≥ 3X		≥ 4X		≥ 5X	
Day	14	28	14	28	14	28	14	28	14	28	14	28
T1	13.7	25.5	25.5	29.4	60.8	45.1	41.2	27.5	29.4	17.6	25.5	11.8
T2	23.5	23.5	5.9	19.6	70.6	56.9	51.0	41.2	39.2	31.4	33.3	19.6
T3	11.5	28.8	25.0	11.5	63.5	59.6	50.0	46.2	46.2	34.6	28.8	25.0

M. haemolytica bacterin-leukotoxoid[b] appeared to be an anamnestic response to the dose administered at day 0; however, the greater antibody response could also be due to a more mature immune system.

Challenge studies are needed to further understand the impact antigen interference has on subsequent disease prevention.

BRSV Vaccination Responses

Calves in this study had BRSV antibody levels prior to vaccination, which was assumed to result from maternal antibody transfer since they were already present by 30 days-of-age. The herd's annual pre-breeding vaccination program did not include a BRSV antigen; thus, stimulation of the cow's immune system and subsequent transfer of BRSV antibodies to the colostrum likely resulted from BRSV virus infection in the adult herd. Prevalence studies suggest BRSV exposure is commonly found in cattle populations.[2,5,11,13,20]

Multiple studies have shown a lack of detectable antibody responses in calves following BRSV vaccination if maternal antibody is present.[1,3,11,12] More recent studies have demonstrated that, in spite of the absence of detectable antibody responses, immune stimulation occurred in intranasally BRSV-vaccinated calves by development of memory B-cells,[12] cell mediated immunity,[8] and upon subsequent challenge.[12,16] However, the ability of MLV BRSV vaccines to stimulate immunity in calves with maternal antibody has been inconsistent.[7] The present study demonstrated two important points when using intranasal BRSV vaccine: 1) ability of the vaccine to stimulate B-cell memory detected 90 days after vaccination as demonstrated by the significant increase in BRSV antibody in calves previously vaccinated, compared to calves vaccinated against BRSV only on day 91; and 2) confirmation that injectable MLV BRSV vaccination can stimulate a systemic anamnestic response in calves previously administered an intranasal vaccine (Table 1).

Conclusions

This study demonstrated that beef calves concurrently vaccinated with *M. haemolytica* and intranasal

virus vaccines mounted an immunologic response similar to calves vaccinated with *M. haemolytica* bacterin-leukotoxoid alone. This information helps define how protocols might be designed to maximize the immune response to both viral and bacterial vaccinations.

Endnotes

[a]PregGuard® GOLD™ FP™ 10, Pfizer Animal Health, New York, NY
[b]One Shot®, Pfizer Animal Health, New York, NY
[c]TSV-2®, Pfizer Animal Health, New York, NY
[d]INFORCE™ 3, Pfizer Animal Health, New York, NY
[e]Bovi-Shield GOLD® 5, Pfizer Animal Health, New York, NY
[f]Ultrabac® 7/Somubac®, Pfizer Animal Health, New York, NY
[g]Dectomax® Pour-On, Pfizer Animal Health, New York, NY
[h]Dr. Daniel Weigel of Outcomes Research Group, Pfizer Animal Health, Kalamazoo, MI
[i]SAS, Version 8.2, SAS Institute Inc., Cary, NC

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