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Passively Transferred Immunity in Newborn Calves, Rate of Antibody Decay, and Effect on Subsequent Vaccination with Modified Live Virus Vaccine

J. Kirkpatrick, *DVM, DABVP*[1], **R.W. Fulton,** *DVM, PhD*[2], **L.J. Burge,** *MS*[2], **W. R. Dubois,** *DVM, DABVP*[1], **M. Payton,** *PhD*[3]
[1]*Department of Veterinary Clinical Sciences*
[2]*Department of Infectious Diseases and Physiology*
College of Veterinary Medicine
[3]*Department of Statistics*
Oklahoma State University, Stillwater, OK 74078

Abstract

The passive immunity transferred to calves via colostrum containing antibodies to infectious bovine rhinotracheitis virus (BHV-1), bovine viral diarrhea virus (BVDV) 1, BVDV 2, parainfluenza-3 virus (PI-3V) and bovine respiratory syncytial virus (BRSV) was investigated to determine half-life of antibody, time to seronegative and effect on immunization. Thirty dairy calves were fed colostrum from non-pooled sources. Serum samples were obtained at the following times: prior to colostral feeding for BVDV isolation; two days of age to measure peak or near peak serum IgG and antibody to the five viruses in this study; and 30 days of age, and approximately 30-day intervals thereafter to assess colostral antibody decay and/or serologic response to vaccine antigen. Antibody titers to each of the five viruses were determined using viral neutralization tests. The mean titers in the day 2 serums were: 17.0 to IBRV; 79.1 to BVDV 1; 297.1 to BVDV 2; 479.2 to PI-3V; and 347.5 to BRSV. The mean half-life of antibodies to each virus was: IBRV, 12.7 days (d); BVDV 1, 20.5 d; BVDV 2, 20.5 d; PI-3V, 21.7 d; and BRSV, 28.1 d. The calculated time to seronegative status for each virus was: IBRV, 65.1 d; BVDV/1, 117.7 d; BVDV/2, 94.0 d; PI-3V, 183.8 d; and BRSV, 200.2 d. The time to seronegative status was dependent on amount of antibody absorbed and antibody decay rate. Calves were vaccinated as viral antibody titers either reached 0, or in the presence of waning antibodies, with a modified live virus vaccine containing IBRV, BVDV 1, BVDV 2, PI-3V, and BRSV immunogens. The active immune response (seroconversion) was dependent on the virus and amount of passive antibodies present at vaccination.

Résumé

L'immunité passive transmise aux veaux par le colostrum contenant des anticorps contre le virus de la rhinotrachéite bovine infectieuse (IBR-1), les virus de la diarrhée virale bovine BVD 1, BVD 2 et parainfluenza –3 (PI-3) et le virus respiratoire syncytial bovin (BRS) a été examinée dans le but de déterminer la demi-vie de l'anticorps, le temps pour atteindre une sérologie négative et l'effet sur l'immunisation. Trente veaux laitiers ont été nourris avec du colostrum de sources différentes. Des échantillons de sérum ont été obtenus aux temps suivants : juste avant la prise du colostrum pour l'isolation du virus BVD; à deux jours d'âge pour mesurer la concentration maximale ou quasi maximale des immunoglobulines G (IgG) et des anticorps des cinq virus de cet étude; et à 30 jours d'âge et par période d'environ 30 jours par la suite pour évaluer la dégradation des anticorps colostraux et/ou la réaction sérologique aux antigènes des vaccins. Les titres d'anticorps pour les cinq virus ont été déterminés avec des tests de neutralisation virale. Les titres moyens au jour 2 étaient les suivants : 17.0 pour le virus IBR, 79.1 pour le virus BVD 1, 297.1 pour le virus BVD 2, 479.2 pour le virus PI-3 et 347.5 pour le virus BRS. La demi-vie moyenne des anticorps pour les cinq virus était de 12.7 jours pour le virus IBR, 20.5 jours pour le virus BVD 1, 20.5 jours pour le virus BVD 2, 21.7 jours pour le virus PI-3 et 28.1 jours pour le virus BRS. Le temps

calculé pour atteindre un statut de sérologie négative était de 65.1 jours pour le virus IBR, 117.7 jours pour le virus BVD 1, 94.0 jours pour le virus BVD 2, 183.8 jours pour le virus PI-3 et 200.2 jours pour le virus BRS. Le temps pour atteindre un statut de sérologie négative était dépendant de la quantité d'anticorps absorbée et du taux de dégradation des anticorps. Les veaux ont été vaccinés, lorsque les titres d'anticorps viraux atteignirent la valeur de 0 ou lorsque la présence des anticorps était moins prononcée, avec des vaccins de virus vivants modifiés contenant des immunogènes IBR, BVD 1, BVD 2, PI-3 et BRS. La réaction immunitaire active (séroconversion) était dépendante du type de virus et de la quantité d'anticorps passifs présente lors de la vaccination.

Introduction

Immunity is passively transferred to newborn calves by ingestion and absorption of antibodies from the dam's colostrum. Ruminants have synepitheliochorial placentation which prevents transfer of maternal immunoglobulins (Ig) prenatally.[1] The Ig are absorbed via the intestinal tract which occurs in the first 24 hours of life, after which the gut closes to further Ig absorption.[7,26]

The duration of the passively acquired Ig from the dam in the calf's serum is dependent on the amount of Ig consumed and the efficiency of absorption within the first 24 hours of life.[18] The decline in passively acquired antibody levels (half-life) varies between Ig classes: 16-32 days for IgG1 and IgG2; 4 days for IgM; and 2.5 days for IgA.[14] The IgG1 is the predominant Ig isotype in colostrum and also predominates in the serum after transfer.[21]

Calves receive passive immunity from their seropositive dams with viral antibodies, including those to infectious bovine rhinotracheitis virus (IBRV), also referred to as bovine herpesvirus-1 (BHV-1), bovine viral diarrhea virus (BVDV) and bovine respiratory syncytial virus (BRSV).[9,10] Early calfhood protection against disease caused by IBRV, BVDV and BRSV is by passive immunity.[3,9] Studies have shown that passive immunity may block the active immune response when the calves receive viral vaccines.[16] Other investigators have shown that some immunogens produce the development of immunologic memory that is not susceptible to maternal antibody regulation.[6,24]

The purpose of the study was (1) to determine the half-life of IBRV, BVDV 1 and 2, PI-3V and BRSV antibodies in calves fed colostrum; (2) to determine the time to 0 titers to IBRV, BVDV 1 and 2, PI-3V and BRSV antibodies in calves fed colostrum; and (3) to evaluate the response of calves with and without detectable maternal antibodies to a modified live virus (MLV) IBRV, BVDV 1 and 2, PI-3V AND BRSV vaccine.

Materials and Methods

Animals. Thirty Holstein dairy calves born between September 1 and November 5 were used in the study. The cows in this herd had not received any viral vaccines within the previous 18 months. Prior to that time, cows were administered a combination vaccine containing chemically altered IBRV and PI-3V, killed BVDV, and modified live BRSV at the end of lactation. Replacement heifers were administered this same vaccine at preweaning, weaning and prebreeding on an ongoing basis.

Calves were removed from their dams immediately after birth and prior to nursing to allow pre-colostral serum sampling. Pre-colostral serums were collected from each calf (0 hour). Calves were then fed two quarts of colostrum at 2.9 (± 1.1) hours postpartum by nipple bottle, followed by two more quarts 11.9 (± 3.2) hours later. Each calf received first milking colostrum from a different cow (30 Holstein cows were colostral sources for this study). Calf #909 nursed its dam prior to pre-colostral blood sample collection. The calves were housed in individual hutches until weaning at six weeks of age, but were in close proximity to each other.

After weaning, the calves were sorted into two groups according to calf size and age to prevent excessive competition for feed, and housed in larger pens. Blood samples were collected at 2 and 30 days of age. The bleeding and vaccination dates thereafter reflect actual age (Table 1). Calves #56, #59 and #906 served as controls and sentinels for the study, did not receive viral vaccine and were monitored for viral infection (IBRV, BVDV 1, BVDV 2, PI-3V and BRSV) by serology at approximately 30-day intervals throughout the study.

Serums. Pre-colostral serums (0 hour) from each calf were used for BVDV isolation using a monolayer enzyme-linked immunosorbent assay (M-ELISA).[25] Serum samples for IgG quantification and viral serology were collected from each calf at two days of age. Subsequently, serum was collected for viral serology from each calf at 30 days of age, and then at approximately 30 day intervals to establish colostral viral antibody decay rates, time to non-detectable levels or low levels, and/or response to a multi-component MLV vaccine containing IBRV, BVDV 1, BVDV 2, PI-3V and BRSV antigens (Table 1). Quantification of IgG in the day 2 sample from each calf was done by radial immunodiffusion (RID) using a commercial kit (Table 1).[a] Serum IgG concentration was classified as adequate (>1600 mg/dl), marginal (800 to 1600 mg/dl) or inadequate (<800 mg/dl).[28]

[a]Triple J Farms, 777 Jorgensen Place, Bellingham, WA 98226
[b]Titanium™ MLV Cattle Vaccines, Agri Laboratories, LTD., St. Joseph, MO 64503

Table 1. Colostral IgG level at 48 hours and colostral antibody level against IBRV, type 1 and type 2 BVDV, PI-3V and BRSV beginning at 2 days (48 hours) of age and at specified times to measure antibody half-life and response to a multicomponent viral vaccine.

Calf ID/ IgG**	Day	BVD 1	BVD 2	IBR	PI3	BRSV
898	2	128	4096	70	256	512
3024	30	64	2048	48	128	
	60	16	1024	13	64	64
	146	0	32			
	169	0		0	0	8
	183*	0	8	0	0	0
	209	32	8	84	0	4
902	2	128	64	0	512	256
2627	30	128	0	0		128
	60	64	8			
	87	16	8			
	101*	8	4	0	128	16
	133	4	1024	14	16	0
906	2	0	0	0	1024	512
1391	30	0	0			
	60	0	0			
	96	0	0		64	
	121	0	0	0	16	8
	133	0	0	0	0	0
910	2	8	0	0	64	256
1391	30	0	0			
	52*	0	0	0	16	32
	84	16	16	0	4	8
53	2	16	4	20	1024	8
2252	30	8	0	0		4
	60	8	0		4	0
	102	0	0			
	116*	0	0	0	4	0
	148	256	64	23	0	8
57	2	128	64	0	256	1024
2282	30	32	16		64	64
	60	16	8		64	32
	91	4	0		16	
	128	0	0	0	4	8
	142*	0	0	0	0	4
	168	64	8	129	0	0
61	2	64	16	16	512	128
2617	30	32	4	14		128
	63*	16	0	0	128	64
	95	64	256	0	16	16
65	2	16	8	0	128	64
472	30	8	0			4
	58*	4	0	0	16	0
	90	32	16	14	8	0

Calf ID/ IgG**	Day	BVD 1	BVD 2	IBR	PI3	BRSV
899	2	0	0	0	512	128
3024	30	0	0	0		128
	60	0	0	0		64
	104*	0	0	0	8	32
	144	256	256	68	0	0
903	2	8	0	10	512	256
2627	30	4	0	0		
	60	4	0		128	16
	90	0	0			
	121*	0	0	0	4	4
	158	64	64	40	0	0
907	2	128	32	0	128	128
1966	30	16	16			
	60	16	4			
	69*	8	4	0	16	64
	101	8	64	204	4	8
911	2	64	8	19	256	512
893	30	16	4	11		
	51*	16	4	0	32	128
	83	8	512	0	0	32
54	2	0	0	0	256	512
3024	30	0	0	0		64
	60	0	0		64	32
	100	0	0			
	106*	0	0	0	4	16
	140	64	256	65	0	16
58	2	0	0	0	1024	256
1966	30	0	0			128
	58*	0	0	0	512	64
	98	128	16	59	32	128
62	2	128	16	20	256	8
2282	30	32	4	14		8
	63*	8	0	0	32	8
	95	32	32	0	4	0
66	2	64	16	38	128	1024
1966	30	64	8	15		128
	60	8	8	0		128
	102	0	0	0	8	32
	116*	0	0	0	4	16
	142	16	0	34	0	4

Calf ID/ IgG**	Day	BVD 1	BVD 2	BHV 1	PI 3	BRSV
900	2	64	16	17	8	64
1265	30	32	8	0	8	32
	60	4	0		0	
	90	0	0			
	130*	0	0	0	0	16
	167	64	64	27	0	0
904	2	0	0	0	64	16
100	30	0	0	0		16
	76	0	0			
	85*	0	0	0	4	4
	121	64	64	109	0	0
908	2	0	0	0	1024	1024
2971	30	0	0			
	57*	0	0	0	256	64
	91	64	64	98	4	0
912	2	256	32	39	1024	1024
1966	30	64	16	19		
	62	16	4	0		256
	99	4	0	0	8	32
	113*	4	0	0	4	8
	139	8	64	14	0	4
55	2	16	0	0	512	64
3444	30	8	0	0		16
	60	4	0		128	
	86	0	0			
	126*	0	0	0	16	16
	163	64	64	0	4	0
59	2	16	4	0	256	512
1391	30	4	0			64
	57	0	0			
	91	0	0			
	114	0	0	0	4	4
	154	0	0	0	0	8
63	2	64	16	16	512	128
893	30	64	4	14		128
	62*	8	0	0	128	128
	94	8	32	0	4	32

Calf ID/ IgG**	Day	BVD 1	BVD 2	BHV 1	PI3	BRSV
901	2	0	0	0	512	128
3024	30	0	0	0		
	60	0	0			16
	94*	0	0	0	8	8
	128	512	64	109	4	4
905	2	0	0	0	1024	512
2252	30	0	0			
	60	0	0			
	79*	0	0	0	32	64
	113	64	32	124	8	4
909	2	128	64	26	256	1024
1391	30	32	16	10		
	65	8	0	0		
	102	4	0	0	4	64
	116*	0	0	0	0	8
	142	8	0	37	0	4
52	2	0	0	0	32	8
266	30	0	0	0	8	0
	60	0	0	0	4	0
	108	0	0	0	0	0
	114*	0	0	0	0	0
	148	512	512	72	4	8
56	2	0	0	0	256	16
1391	30	0	0		64	4
	60	0	0		16	0
	94	0	0		4	0
	131	0	0	0	0	0
	145	0	0			
	171	0	0	0	0	0
60	2	0	0	0	1024	256
1966	30	0	0			64
	55*	0	0	0	64	32
	89	32	64	126	32	64
64	2	0	0	0	1024	64
2671	30	0	0			8
	50*	0	0	0	128	16
	84	16	8	62	32	4

*Age of calf (days) at vaccination
**IgG in mg/dl at 48 hours

Serology. A microtiter virus neutralization test (VNT) in Madin-Darby bovine kidney cells (MDBK) in 96-well plates was used to quantitate viral neutralizing antibodies to BVDV types 1 and 2, PI-3V and BRSV.[11,13] The viruses used in the VNT were CP BVDV type 1 Singer strain; CP BVDV type 2 125C strain; PI-3V, SF-4 strain; and BRSV vaccinal strain. The lowest dilution tested was 1:4.

A plaque reduction assay (PRA) was used to detect viral neutralizing antibodies to BHV-1 using the Cooper strain as the challenge virus in 24-well plates with MDBK cells.[11,13] The lowest dilution tested was 1:10.

Serums were considered negative (0) if there was no neutralization at 1:4, the lowest dilution tested in the microtiter VNT, or no neutralization at 1:10, the lowest dilution tested with the PRA. The negative (0) antibody level was converted to 1 for the $\log_2$ used in the statistical analysis, i.e., titers of 4, 8, and 16 converted to $\log_2$ numbers of 2, 3, and 4, respectively. Reciprocals of the endpoint titers are reported in the text and tables.

Vaccination. Maternal viral antibody decay in each calf was followed to either low or non-detectable levels, at which time 27/30 calves were administered a MLV vaccine by the intramuscular route. The vaccine was from a single lot number and contained five viral antigens; IBRV, BVDV 1, BVDV 2, PI-3V and BRSV (Table 3).[b] The antibody level to each of the five viruses varied from 0 to positive titers of different levels. The age of the calves at vaccination ranged from 50 to 183 days (60 days ± 4 days; 90 ± 10.5 days; 120 ± 8.3 days; 183 days). Serum samples were collected from calves at 32 (± 4) days after vaccination. Serums collected at vaccination and post-vaccination were tested for viral antibodies as described above. Seroconversion was defined as a four-fold or greater increase in antibody for BVDV 1, BVDV 2, PI-3V or BRSV. Increases of only one dilution from 0 to 4 were not considered seroconversion to these viruses. Seroconversion to IBRV was considered ≥ 1:20 in the PRA as all were 0 at vaccination.

Statistical analysis. For each animal and virus a simple linear regression was performed using PROC REG and SAS Version 6.11 with day as the independent variable and the titer level as the response. Initial serum collection was on day 2, and subsequently, serums were collected at 30 days of age, and at approximately each 30 days thereafter from each animal until the calf became 0 for the respective virus or the date the calf was vaccinated. Regressions were used to estimate half-life and the time required for the calf to become negative (0) for the respective viral antibody. These estimates were then compared in an analysis of variance using PROC GLM in SAS to examine whether the average half-life or the average times required to become negative were equal for the five viruses. If the five viruses were declared significant in the analyses of variance, Fisher's Least Significant Difference procedure was used to declare significant differences among the viruses. For each virus, the rates of seroconversion for the seropositive and seronegative calves at vaccination were compared using the FISHERS EXACT TEST.

Results

Monitoring for viral infections. There was no evidence of active infection with IBR, BVDV 1, BVDV 2, PI-3V or BRSV in this study. No calves displayed clinical signs of disease during the study. None were persistently infected with the BVDV as the 0 hour sera were all negative for the virus by the M-ELISA procedure. There was no measured seroconversion in the three control calves, #56, #59 and #906, to any of the five viruses. The other 27 calves either remained seronegative to the respective viruses, or the passively transferred antibody to the respective virus continued to decline at the expected rate to non-detectable or low levels (Table 1).

Antibody levels transferred via colostrum. All calves except #909 were antibody negative to the five viruses prior to feeding colostrum. This animal was discovered later to have nursed its dam immediately after calving and prior to blood collection for the pre-colostral sample. The calf had similar antibody titers in both the 0 hour and day 2 samples for each virus. This animal was kept in the study since the starting point was at or near the peak of serum IgG. Source of the colostrum was from the same herd as the remainder of the calves in this study.

Nineteen calves had adequate transfer of IgG (1966 to 3024 mg/dl), 8 calves had marginal transfer of IgG (893 to 1391 mg/dl) and 3 calves had inadequate transfer (100 to 472 mg/dl; Table 1).

The number of calves with passively derived viral antibodies in the day 2 samples, and the level of antibody titers in seropositive calves varied among viruses (Table 1). The number of calves seropositive, the geometric mean titers and range of titers for those seropositive calves for each virus were: IBRV, 11/30, mean of 26.5(10-70); BVDV 1, 18/30, mean of 79.1 (8-256); BVDV 2, 15/30, mean of 297.1 (4-4096); PI-3V, 30/30, mean of 479.2 (8-1024); and BRSV, 30/30, mean of 347.5, (8-1024; Table 2).

Antibody half-life. The half-life of the colostral derived antibodies to the five viruses were 12.7 d for IBRV, 20.5 d for BVDV 1, 20.5 d for BVDV 2, 21.7 d for PI-3V and 28.1 days for BRSV. Assuming that the half-life of the antibodies are normally distributed, analysis of variance techniques show that there were significant differ-

Table 2. Number of seropositive colostrum-fed calves, day 2 mean titers and ranges, antibody half-life, and estimated time to seronegative status to IBRV, BVDV 1 and 2, PI-3V and BRSV (mean ± SD in days).

Virus	No. seropositive	Day 2 (mean titers and ranges)	Half-life (mean ± d)	Time to 0 (mean ± d)
IBRV	11	26.5 (10-70)	12.7 ± 5.5[a]	65.1 ± 37.8[a]
BVDV1	18	79.1 (8-256)	20.5 ± 6.2[ab]	117.7 ± 37.7[a]
BVDV2	15	297.1 (4-4096)	20.5 ± 12.4[ab]	93.9 ± 61.9[a]
PI-3V	30	479.2 (8-1024)	21.7 ± 9.6[b]	183.8 ± 100.0[b]
BRSV	30	347.5 (8-1024)	28.1 ± 19.4[b]	200.2 ± 116.7[b]

[a,b]Values with the same superscript do not differ ($p < .05$).

Table 3. Serologic response of calves to a 5-component MLV vaccine administered when maternal antibody titers for each component were at 0 or low.

		Prevaccination/32-day* post-vaccination titers				
Calf ID	**Calf age at vaccination (days)****	**BVDV1**	**BVDV2**	**IBRV**	**PI3V**	**BRSV**
898	183	0/32	8/8	0/84	0/0[c]	0/4[c]
899	90	0/256	0/256	0/68	8/0	32/0
900	120	0/64	0/64	0/27	0/0[c]	16/0
901	90	0/512	0/64	0/109	8/4	8/4
902	90	8/4	4/1024[b]	0/14	128/16	16/0
903	120	0/64	0/64	0/40	4/0	4/0
904	90	0/64	0/64	0/109	4/0	4/0
905	90	0/64	0/32	0/124	32/8	64/4
907	60	8/8	4/64[b]	0/204	16/4	64/8
908	60	0/64	0/64	0/98	256/4	64/0
909	120	0/8	0/0[c]	0/37	0/0[c]	8/4
910	60	0/16	0/16	0/0[c]	16/4	32/8
911	60	16/8	4/512[b]	0/0[c]	32/0	128/32
912	120	4/8[a]	0/64	0/14	4/0	8/4
52	120	0/512	0/512	0/72	0/4[c]	0/8[b]
53	120	0/256	0/64	0/23	4/0	0/8[b]
54	90	0/64	0/256	0/65	4/0	16/16
55	120	0/64	0/64	0/0[c]	16/4	16/0
57	150	0/64	0/8	0/129	0/0[c]	4/0
58	60	0/128	0/16	0/59	512/32	64/128[a]
60	60	0/32	0/64	0/126	64/32	32/64[a]
61	60	16/64[b]	0/256	0/0[c]	128/16	64/16
62	60	8/32[b]	0/32	0/0[c]	32/4	8/0
63	60	8/8	0/32	0/0[c]	128/4	128/32
64	60	0/16	0/8	0/62	128/32	16/4
65	60	4/32[b]	0/16	0/14	16/8	0/0[c]
66	120	0/16	0/0[c]	0/34	4/0	16/4

*Mean age in days 32 ± 4

**Mean age in d (± SD): 60 ± 4; 90 ± 10.5; 120 ± 8.3; 183

[a]Denotes a lack of 4-fold seroconversion in the presence of antibody

[b]Denotes a 4-fold serovonversion in the presence of antibody

[c]Denotes a lack of measurable serologic response (>1:4) in the absence of measurable antibody

ences among these half-lives with an overall p-value of 0.0173 (Table 3). Multiple comparisons performed on the half-lives indicate that the mean half-life for IBRV was significantly different from PI-3V and BRSV.

Time to estimated seronegative status. The estimated length of time for calves with colostral antibodies to become seronegative to the five viruses was significant, with an overall p-value of 0.0001. The time required for IBR (65.1 days), BVDV 1 (117.7 days) and BVDV 2 (93.9 days) antibodies to decline to 0 were not significantly different, but they were significantly shorter than for PI-3V (183.8 days) and BRSV (200.2 days; Table 2).

Antibody response to vaccination. Twenty-seven calves were vaccinated with the MLV vaccine. The antibody titer to the respective virus at vaccination varied between viruses (Table 1). The interval between vaccination and serum collection was 32 ± 4 days (Table 3). All 27 calves were seronegative to IBRV at vaccination. Eighteen of the 27 calves seroconverted (0 to >1:20) to IBRV, three had a titer increase (1:20), and 6 calves remained seronegative after vaccination. Since no calves were seropositive at vaccination, no tests of conversion rates were performed.

There were 19/27 calves seronegative to BVDV 1 at vaccination and all 19 calves seroconverted to BVDV 1 after vaccination. Of the remaining 8 calves with the BVDV 1 antibody at vaccination, three calves (one each with titers of 4, 8 and 16) seroconverted, whereas calves with antibody titers of 4 (one calf), 8 (three calves) and 16 (one calf) did not seroconvert (Tables 3, 4). The seropositive calves seroconverted at a lower rate than those that were seronegative at vaccination (p = 0.00069).

Twenty-three of 27 calves were seronegative to BVDV 2 at vaccination. There were 21 BVDV 2 seronegative calves which seroconverted after vaccination, and 2 that did not. There were three calves with BVDV 2 antibody titers of 4, and all three seroconverted. One calf with a titer of 8 did not seroconvert (Table 3). The seroconversion rates of the seropositive and seronegative calves at vaccination did not significantly differ (p = 0.3945; Table 4).

Of the 27 calves, 22 had PI-3V antibodies at vaccination. None of the 22 seropositive calves or 5 seronegative calves seroconverted after vaccination. Since no calves seroconverted, no tests of conversion rates were performed.

Twenty-three of 27 calves were seropositive to BRSV at vaccination, and none of 23 seroconverted following vaccination. Four calves were seronegative at vaccination; two calves seroconverted after vaccination and two calves did not. The calves seropositive at vaccination seroconverted at a lower rate than those that were seronegative at vaccination (p = 0.0171; Table 4).

Discussion

The half-life of viral antibodies in this study were generally similar to those reported in other studies, with the exception of IBRV. Brar *et al* reported that the IBRV and BVDV colostral-conferred antibody half-life in calves was 21 days for each virus.[6] In a subsequent study, Menanteau-Horta, *et al* reported that the average antibody half-life to IBRV and BVDV in colostrum-fed calves was 19 and 20 days, respectively.[24] The IBRV antibody half-life of 12.7 days in this study was approximately six days shorter than reported by Menanteau-Horta *et al*.[24] Potentially the IBRV antibodies in the colostrum were different Ig isotypes with a shorter half-life. This would be unusual as 30 different colostral sources were used in the study. Another difference may be related to variations in the serologic tests used to detect antibodies to IBRV. The relatively low titers (10-70) in the day 2 serum could possibly be a reason for the half-life differential. In future studies, this should be repeated with higher antibody levels at the onset.

The time required for colostral antibodies to decline below detectable levels is dependent on the amount of viral antibody consumed, the amount absorbed from the intestinal tract into the serum and the rate of decay. Also, exposure to field virus could potentially affect the time to become seronegative, but this was not apparent in this study. Several studies have reported

Table 4. The number of seropositive and seronegative calves responding to a MLV IBRV, BVDV 1, BVDV 2, PI-3V and BRSV vaccine with a four-fold or greater than a 0 to 1:4 increase in serum titer for BVDV 1, BVDV 2, PI-3V and BRSV, and greater than a 0 to 1:20 for IBRV.

Virus	Seronegative calves responding[a]	Seropositive calves responding[b]	p value
IBRV	18/27	0/0	NC[c]
BVDV 1	19/19	3/8	0.00069
BVDV 2	21/23	3/4	0.3945
PI-3V	0/5	0/22	NC[c]
BRSV	2/4	0/23	0.0171

[a]Seronegative calves seroconverting/seronegative calves vaccinated.

[b]Seropositive calves seroconverting/seropositive calves vaccinated.

[c]No comparisons can be made.

the duration of colostral antibodies to various viruses.[6,18,24,27] Not all of these studies reported the estimated half-life of the viral antibody investigated.[2,6,27] Results were expressed either as the time the respective antibodies were last detected, or the first negative date. On occasion the dates were expressed as means and/or with ranges. Kendrick and Franti reported that BVD antibodies decayed to undetectable levels by 105-230 days of age.[18] Menanteau-Horta *et al* reported that BVDV antibodies reached 0 at 200 days, and IBRV antibodies reached 0 by around 170 days.[24] For BRSV, Baker *et al* reported that passive antibodies were undetectable in an average of 99 days (range 30-208 days),[2] and van der Poel *et al* reported that BRSV antibody levels in colostrum fed calves dropped to undetectable levels at 3-4 months of age.[27]

In the current study, viral antibody levels of some serums became 0 to a specific virus prior to vaccination, whereas other calves had antibodies at vaccination. The age at which an animal with passively derived antibodies would become negative varied with the virus. The standard deviation (SD) for these means were quite large, ranging from 37.0 to 116.7 days for the five viruses. Also, the SD for the half-life means were often high, ranging from 5.5 to 19.4 days for the five viruses. These data illustrate the variability of data expression, and focuses attention also on the varied amount of colostral antibody fed, the amount of antibody absorbed and the rates of antibody decay.

Vaccination of young calves or neonates is possible for certain immunogens, however the animal may not respond if antibody obtained from the dam is present in the circulation at vaccination.[16] In this study, most calves receiving a MLV vaccine (IBRV, BVDV 1 and BVDV 2) seroconverted. This was due in part to the lack of antibodies to IBRV, BVDV 1 and BVDV 2 at vaccination. Of the calves seronegative to IBRV, BVDV 1 and BVDV 2, 74.1% seroconverted to IBRV, 100% to BVDV 1 and 91.3% to BVDV 2 (Table 3).

Colostral derived antibody may block immunization. In this study, the BVDV 1 seroconversion rate was lower in the seropositive (3/8) than the seronegative (19/19) calves at vaccination ($p = 0.00069$). The antibody titer which appeared to block seroconversion to BVDV 1 were not uniform. There were instances where titers of 4-16 either blocked or did not inhibit seroconversion following BVDV 1 vaccination. Serum titers to BVDV 2 greater than 4 blocked a measurable serologic response to vaccination. However, seroconversion rates of seropositive (3/4) and seronegative (21/23) calves did not significantly differ ($p = 0.395$). These results are somewhat different than two other reports on the response of calves with passive immunity to IBRV and BVDV to MLV vaccination. In the first study, calves seroconverted to BVDV after vaccination when the geometric mean titers were between 20 and 96, but the calves did not seroconvert to IBRV if antibodies were present at the initial vaccination.[6] In the second study, calves with a geometric mean titer of 35 at day 84 serconverted to BVDV after the initial vaccination, but the titer then declined until day 196 when they were revaccinated.[24] The individual calf titer at/or subsequent to vaccination to IBRV was not noted in the article. It is somewhat difficult to compare the results of the current study with the prior studies when ranges of individual titers were not reported.

No calves in our study, with or without PI-3V antibodies, seroconverted following vaccination. Only vaccine from one lot was used in this study, therefore no other comparisons could be made to indicate whether the calves, even those seronegative, would respond to vaccination. Either the maternally derived immunity to PI-3V blocked the immune response to MLV vaccination, or the PI-3V component was a weak immunogen in this vaccine lot. Fulton *et al* reported seroconversion to the PI-3V immunogen following vaccination of seropositive calves (> 1:4) less than one year of age. Three MLV vaccines and one killed virus (KV) vaccine were used in that study.[13]

Calves seronegative to BRSV in our study seroconverted after vaccination with MLV vaccine (2/4) at a significantly higher rate than the seropositive calves (0/23; $p = 0.0171$). This would suggest that maternally derived serum antibodies blocked the humoral immune response to MLV vaccination. Kimman and Westerbrink reported that live attenuated BRSV vaccines were ineffective in calves with maternal antibodies.[20] There was no description of the experimental design/results used to make that determination.

Kaberle *et al* reported on the antibody response of calves with maternal antibody administered KV vaccines.[17] In that study, 28-69 day old calves with maternal antibodies to IBRV, BVDV 1, BVDV 2 and PI-3V received one of three KV vaccines. The mean and range of titers at vaccination for the 120 calves for the respective viruses were: IBRV, mean 14.7 (range of <2-128); BVDV 1, mean 76.6 (range of 20-1920); BVDV 2, mean 45.9 (range of 7.5-1280); and PI-3V, mean 40.8 (range of <2-480). Serums were collected 32 days later, and the antibody titers to all four viruses declined in all three vaccine groups at a rate similar to controls. Calves were revaccinated at that time. Serums were tested 29 days later (day 61 of the experiment) and demonstrated a measurable serologic response to selected vaccines. In this study the response of those calves with higher maternal antibodies were not listed, only mean titers.

In another study using MLV vaccine, calves with maternal antibodies to IBRV did not seroconvert after initial vaccination, but responded with a secondary response after subsequent vaccination with IBRV.[6] In a

more recent study,[10] there was no substantial increase in serum antibody to IBRV and BRSV in calves with maternal antibodies that were vaccinated with a MLV vaccine, yet the calves responded with virus-specific T-cell responses. Potentially, calves with maternal antibodies may be primed for subsequent T-cell responses when vaccinated with MLV vaccine.[10]

Results of this and other studies suggest some important points to consider when developing a health management plan. Plans should be developed on an individual herd/area basis to reduce disease incidence, decrease pathogen concentration and to maximize calf immunity at the time of greatest challenge (neonatal, early calfhood or weaning/postweaning). Colostral antibodies, although a major defense mechanism in the early calfhood period, decay at a fairly constant rate and their longevity is dependent on the quantity of antibodies consumed and efficiency of absorption.[6,18,24,27] Colostral antibodies to IBRV, BVDV and BRSV, while preventing or decreasing the severity of clinical disease, may not prevent infection or block virus transmission, thereby allowing increased concentration of pathogens in the herd.[3,5,14] However, investigators have demonstrated a priming effect on the immune system when calves are exposed to IBRV, BVDV or BRSV antigen in the presence of colostral antibodies. Repeated exposure to these viral antigens has elicited a stronger, more rapid seroconversion.[6,10,24] Our study and others have shown seroconversion to BVDV vaccine or virulent virus when calves have moderate to low levels of passive antibodies.[3,8,24] Therefore, it seems prudent to begin the use of viral vaccines in calves at an early age (~ 60 days), using vaccine manufacturers recommendations. This should either result in seroconversion, prime the immune system, or result in no response, depending on the serologic status of the calf for the specific virus. Repeated vaccination(s), regardless of vaccine type (MLV or KV) is necessary to establish a satisfactory level of immunity in the group.

Appropriate vaccination protocols, vaccine handling and proper administration are only part of a total herd health management program. Without other appropriate health management practices (inter- and intra-herd biosecurity, sanitation, stress management, etc.) in place, the best vaccination program will be less than effective. It is a science that must be used appropriately at various production levels to assist in decreasing disease incidence and increasing productivity.

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