Transfer of specific antibodies against bovine respiratory syncytial virus (BRSV) from maternal colostrum into the respiratory tract of dairy calves and its implication on vaccination programs and animal health

Oscar F. Huertas, DVM, MS
Food Animal Internal Medicine Resident

AUBURN UNIVERSITY
COLLEGE OF
VETERINARY MEDICINE

- The newborn calf has a complete/functional but inexperienced immune system
- Slow to respond to infectious microorganisms
  - Devoid of specific immunity
- Calf needs specific immunity (IgG), Leukocytes, cytokines
  - Colostrum

Chase, C. C., Hurley, D. J., & Reber, A. J. (2008). *Veterinary Clinics of North America: Food Animal Practice*

Maternal colostrum

- IgM 3 – 13 g/L
- IgA 1 – 7 g/L
- **IgG 24 – 100 g/L (> 90% IgG1)**

White blood cells (900 – 2000 cells/uL)

68% Lymphocytes

- **> 90% T lymphocytes**
- < 5% B lymphocytes

Important on activating cell mediated immunity
- Improved cell mediated responses to BVDV
- Reduced *E. coli* shedding

Failure in the transfer of passive immunity (FTPI)

- Inadequate absorption of immunoglobulins from colostrum
- **Dairy calves**:
  - **Serum IgG < 1,000 mg/dL or < 10 g/L**
  - **Significant increase in mortality in calves with serum IgG at 24 h of < 10 g/L**

[Gay et al., 1983; NAHMS Dairy Report 2007; Shivley C. ADSA proceedings 2015]

Reduction of dairy calf morbidity and mortality since 1992 in the U.S.

- Mortality
  - 1991 = 10.8%
  - **2014 = 6.4%!**
- Morbidity
  - 1991 = 36.1%
  - **2014 = 33.9%!**
  - Still BRD and diarrhea!!
- Colostrum management improvement responsible for the changes

[NDHEP 1991; NAHMS 2014]

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Consensus recommendations on calf- and herd-level passive immunity in dairy calves in the United States

J. Lombard,[1]*† N. Urie,[1] F. Garry,[2] S. Godden,[3] J. Quigley,[4] T. Earleywine,[5] S. McGuirk,[6] D. Moore,[7] M. Branan,[1] M. Chamorro,[8] G. Smith,[9] C. Shivley,[1] D. Catherman,[10] D. Haines,[11] A. J. Heinrichs,[12] R. James,[13] J. Maas,[14] and K. Sterner[15]

[1]USDA–Animal and Plant Health Inspection Service–Veterinary Services, Center for Epidemiology and Animal Health, National Animal Health Monitoring System, Fort Collins, CO 80526-8117
[2]Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins 80523-1678
[3]Department of Veterinary Population Medicine, College of Veterinary Medicine, University of Minnesota, St. Paul 55108
[4]Cargill Animal Nutrition, Brookville, OH 45309
[5]Land O'Lakes Animal Milk Solutions, Cottage Grove, WI 53527
[6]School of Veterinary Medicine, University of Wisconsin, Madison 53706
[7]Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Washington State University, Pullman 99164
[8]Department of Clinical Sciences, College of Veterinary Medicine, Auburn University, Auburn, AL 36849
[9]Department of Population Health and Pathobiology, North Carolina State University, Raleigh 27607
[10]Strauss Feeds, Watertown, WI 53908
[11]SCCL, Saskatoon, Saskatchewan, Canada, 57K 6A2
[12]Department of Animal Science, The Pennsylvania State University, University Park 16802
[13]Down Home Heifer Solutions, Blacksburg, VA 24060
[14]School of Veterinary Medicine, University of California, Davis 95616
[15]Sterner Veterinary Clinic P.C., Ionia, MI 48846

	Categories of transfer of passive immunity			
	Excellent	**Adequate**	**Fair**	**Failure**
IgG (g/L)	**> 25**	**18 – 24.9**	10 – 17.9	< 10
Intake of colostrum (g of IgG) to reach standard	**300 g**	**~250 g**	**~200 g**	**< 100 g**

[Adapted from Lombard et al., J Dairy Sci. 2020]

Recommendations to achieve excellent transfer of passive immunity – dairy calves

- A single feeding of colostrum at 2 hours delivering 300g of IgG
  - 4 L of high-quality MC (> 22% Brix)
- Multiple colostrum feedings delivering 400g of total IgG in 24 h
  - 6 L or high-quality MC (>22% brix)
- Commercial colostrum replacer products?

Not just matter of enough colostrum and IgG

- Higher serum IgG or STP at 24 hours well correlated with calf health
- Maternal colostrum provides inconsistent levels and spectrum of specific-neutralizing antibodies
  - Enteric and **respiratory** pathogens

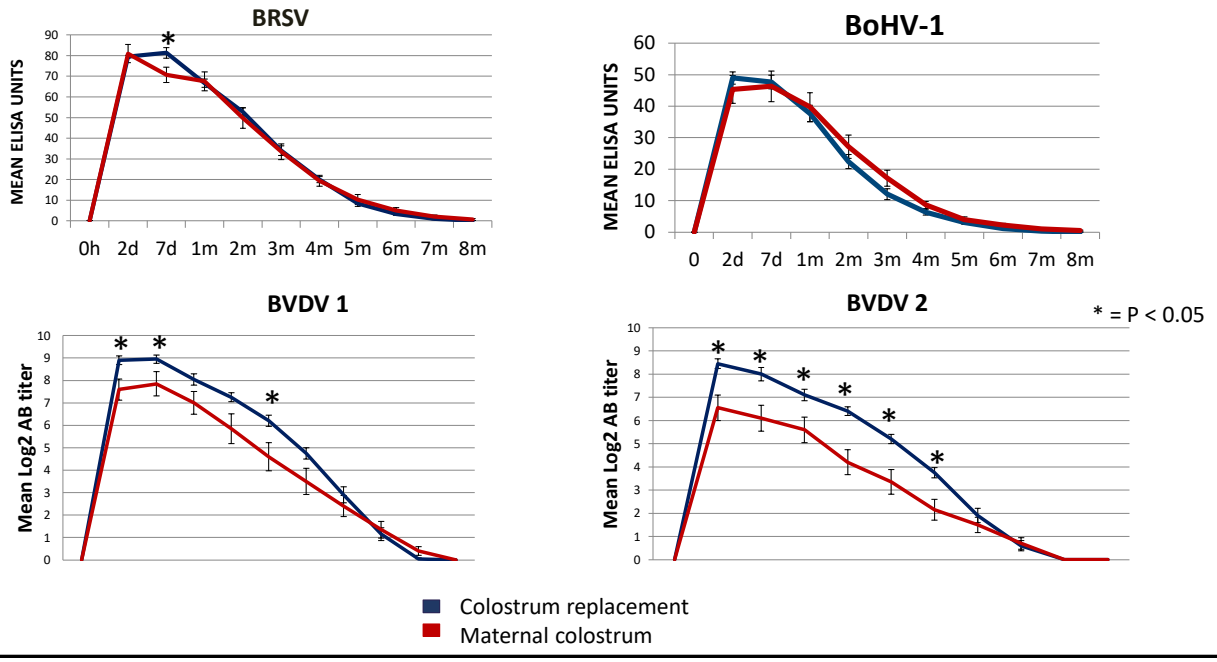
Virus	Kirkpatrick J. Bov Pract 2001 2-day dairy calves	Fulton R. Vaccine 2004 60-day beef calves	Chamorro M. CJVR 2014 2-day dairy calves	Chamorro M. BMC Vet Res 2015 42-day beef calves	Chamorro M. AJVR 2016 90-day beef calves	Reppert E. CJVR 2019 2-day beef calves	Martinez D. AJVR 2022 2-day beef calves
BVDV-1	8 – 256	0 – 16,384	32 – 2,048	1 – 4,096	1 – 1,024	16 - 4,096	
BVDV-2	4 – 4,096	0 – 8,192	4 – 2,048	1 – 4,096	1 – 512	32 – 4,096	
BRSV	8 – 1,024	8 – 4,096	26 – 119*				1 – 596
BoHV-1	0 – 70	0 - 935	11 – 85*		1 - 128	0 - 256	
PI3V	8 – 1,024	8 – 2,048	22 – 168*				*Elisa OD values

Virus	Mean time to reach sero-negative status (days)
BVDV 1	117-185.6
BVDV 2	94-165
BRSV	**30-186.7**
BoHV-1	123-170
PI3V	190-200

Comparison of levels and duration of detection of antibodies to bovine viral diarrhea virus 1, bovine viral diarrhea virus 2, bovine respiratory syncytial virus, bovine herpesvirus 1, and bovine parainfluenza virus 3 in calves fed maternal colostrum or a colostrum-replacement product

Manuel F. Chamorro, Paul H. Walz, Deborah M. Haines, Thomas Passler, Thomas Earleywine, Roberto A. Palomares, Kay P. Riddell, Patricia Galik, Yijing Zhang, M. Daniel Givens

Canadian Journal of Veterinary Research **2014; 8:81**



- Specific immunity against respiratory viruses provided by colostrum to newborn calves varies in levels and duration. This can open a window of opportunity for infectious disease

BRSV

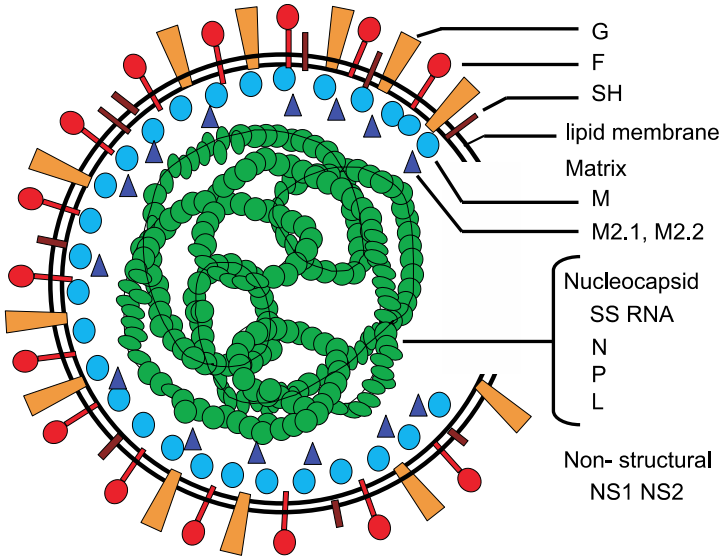


Figure 1. Diagram of bovine respiratory syncytial virus.

Epidemiology

- Worldwide distribution
- Sero-prevalence in the US
  - Weaning calves: 28%
  - Yearlings: 49%
  - Adult cows: 70%
- Morbidity 60-80%
  - Calves < 6 months of age most commonly affected
- Mortality: up to 20% in some cases

[Collins JK, et al. Am J Vet Res 1988; Valarcher J.F. and Taylor G., Vet Res. 2017]

Clinical signs

- Fever 40ºC (days 2-6 pi)
- Repeated spontaneous cough
- Nasal discharge
- Tachypnea

- Dyspnea
- Respiratory distress
  - Severe interstitial pneumonia
  - Death

Natural occurrence of BRSV

- Seasonal yearly outbreaks
  - Young dairy calves
  - High morbidity - low mortality
    - High mortality rates in some cases (20%!!)
  - Repeated exposure overtime reduces severity
    - Persistence or re-introduction??

[Baker, et al. Am J Vet Res 1986; Kimman et al., Vet Rec 1988; Schreiber et al., J Vet Med B 2000; Larsen et al., Acta Vet Scand 2001]

BRSV intranasal vaccination with modified-live virus (MLV) vaccines

Study	Study pop.	Vaccine/ route/ doses	Age at vacc.	Challenge (days after vacc.)	Morbidity	Mortality	BRSV shedding NS
Vangeel, 2007	Dairy calves	**MLV**/IN/1	14d	5d-66d	↓	No effect	↓
Ellis, 2007	Dairy calves	MLV/IN/1-2	14d-60d	8d-21d	↓	-	↓
Ellis, 2010	Dairy calves	**MLV**/IN-SC/1	**3-8d**	21d-135d	135d no effect	-	↓
Ellis, 2013	Dairy calves	**MLV**/IN/1	**3-11d**	49d-105d	↓	-	No effect
Ellis, 2018	Beef calves	Comb MLV IN/KV MLV IN/MLV -/SC MLV	**Birth 1st dose** 60d 2nd dose	120d After 2nd dose	No effect	No effect	No effect
Kolbe, 2019	Dairy calves	**MLV**/SC/1	30d	90d	↓	-	↓

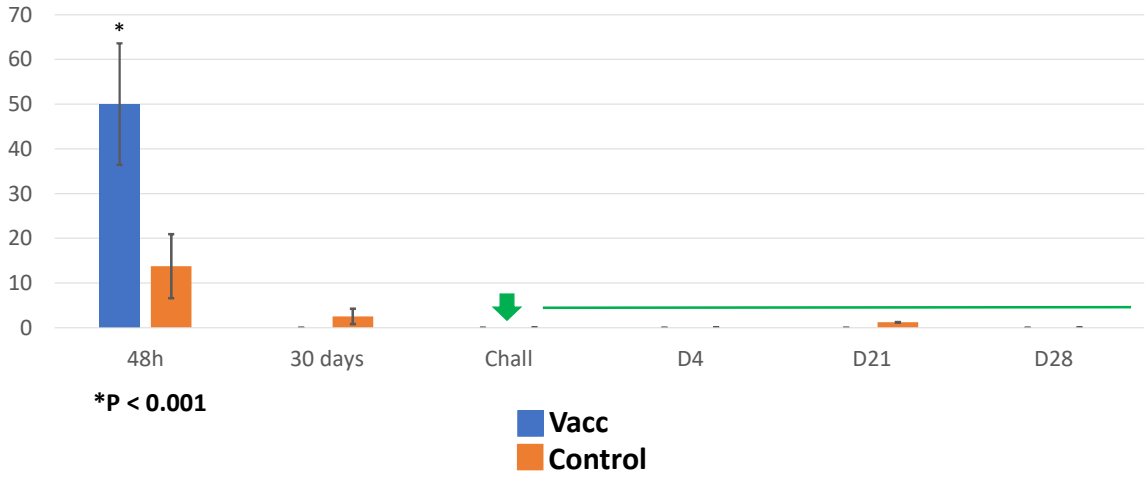
AJVR

AVMA

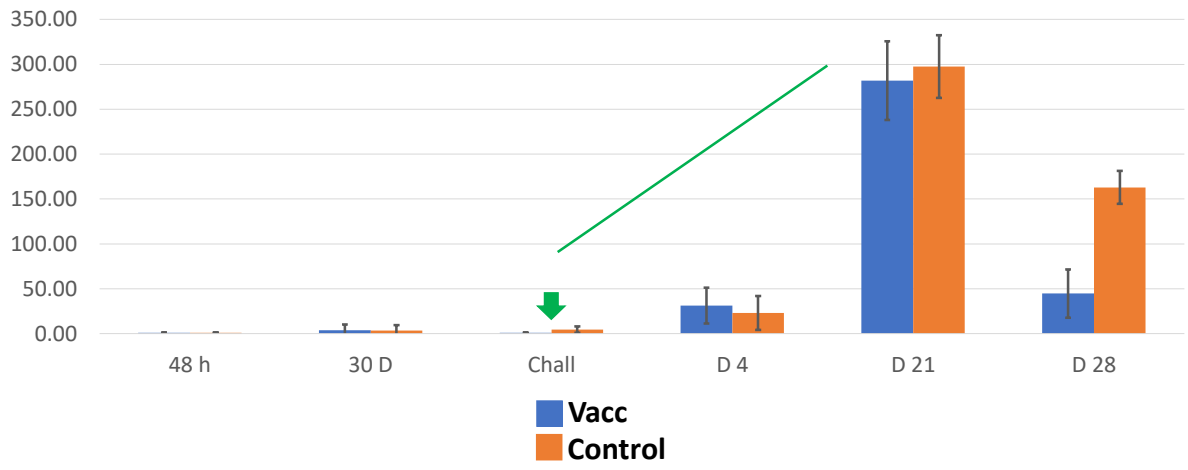
The titers, duration, and residual clinical protection of passively transferred nasal and serum antibodies are similar among beef calves that nursed colostrum from vaccinated or unvaccinated dams and were challenged experimentally with bovine respiratory syncytial virus at three months of age

David A. Martínez, DVM, MS[1]; Manuel F. Chamorro, DVM, MS, PhD, DACVIM[1]*; Thomas Passler, DVM, PhD, DACVIM[1]; Laura Huber, DVM, MS, PhD, DACVPM[2]; Paul H. Walz, DVM, MS, PhD, DACVIM[2]; Merrilee Thoresen, PhD[3]; Gage Raithel, BS[2]; Scott Silvis, MS[2]; Ricardo Stockler, DVM, PhD, DABVP-Dairy[1]; Amelia R. Woolums, DVM, MS, PhD, DACVIM, DACVM[3]

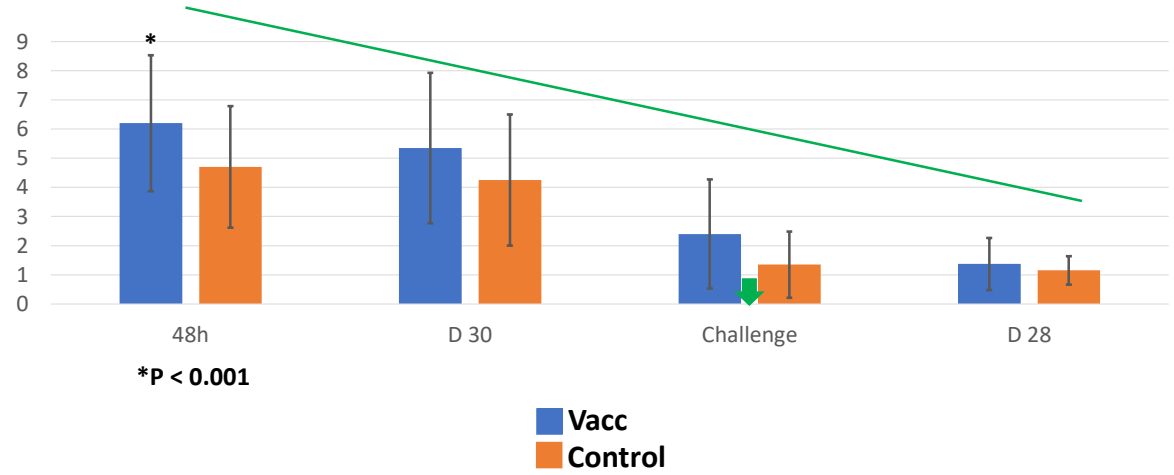
Mean nasal BRSV-IgG-1 titer



Mean nasal BRSV-IgA-1 titer



Mean Log2 BRSV serum neutralizing antibodies



veterinary sciences

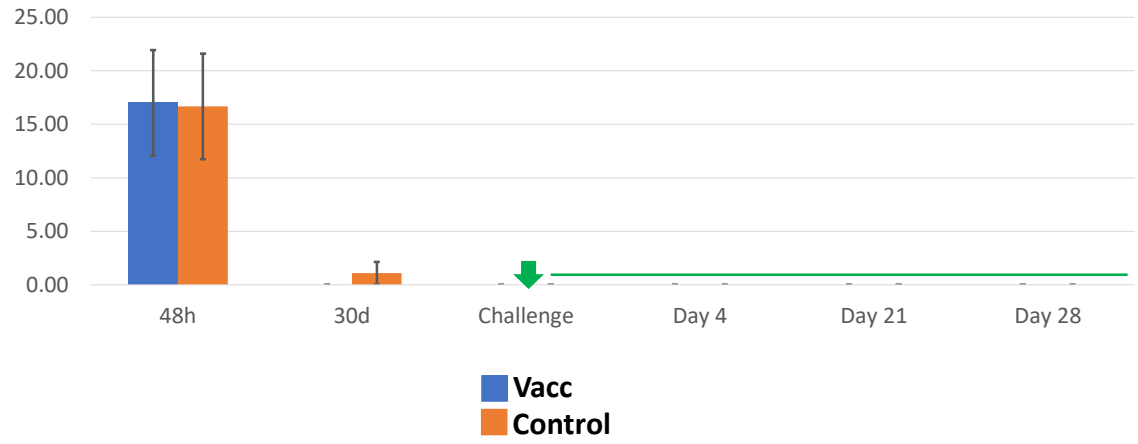
MDPI

Article

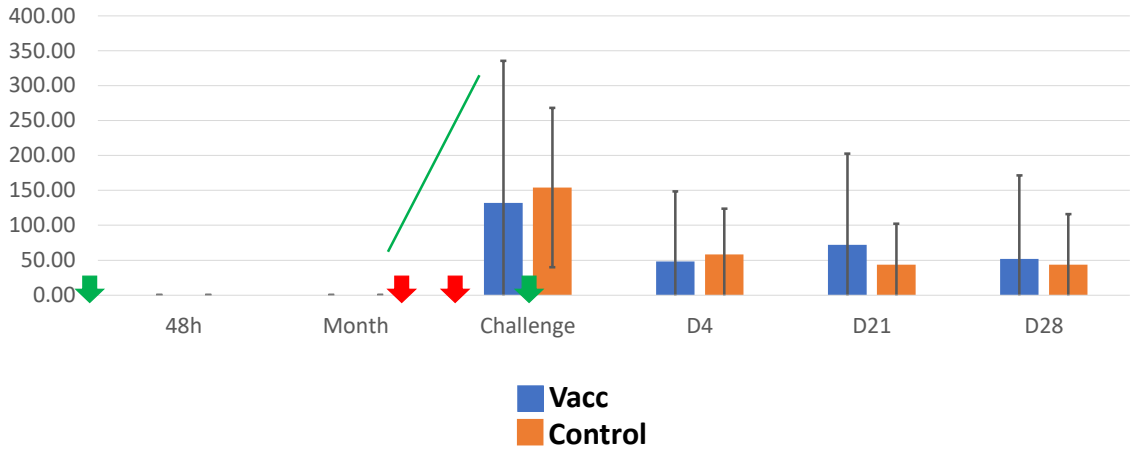
Local and Systemic Antibody Responses in Beef Calves Vaccinated with a Modified-Live Virus Bovine Respiratory Syncytial Virus (BRSV) Vaccine at Birth following BRSV Infection

David A. Martínez [1], Manuel F. Chamorro [1,*], Thomas Passler [1], Laura Huber [2], Paul H. Walz [2], Merrilee Thoresen [3], Gage Raithel [2], Scott Silvis [2], Ricardo Stockler [4] and Amelia R. Woolums [3]

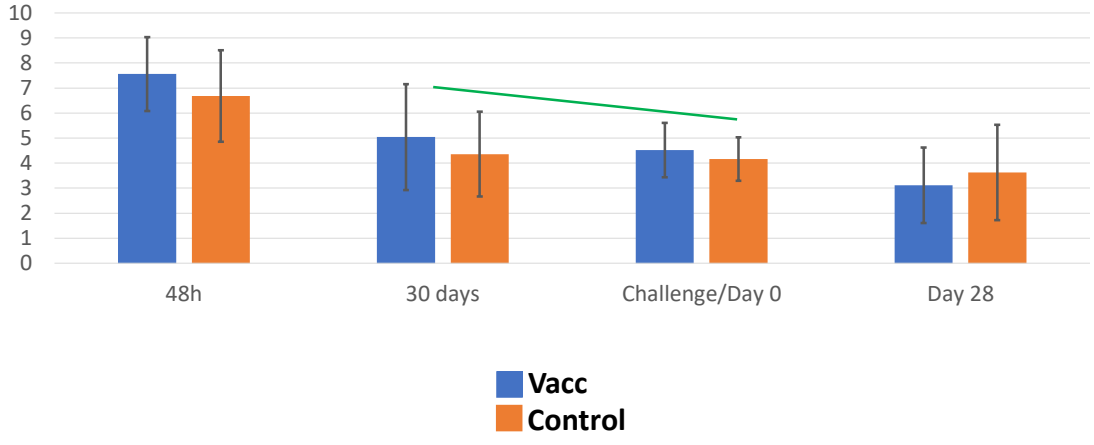
Mean nasal BRSV-IgG-1 titer



Mean nasal BRSV-IgA-1 titer



Mean Log2 BRSV serum neutralizing antibodies



Levels and persistence of colostrum-derived nasal and bronchoalveolar fluid (BALF) bovine respiratory syncytial virus (BRSV) immunoglobulin-1 (IgG1) in dairy calves

Huertas OF, Chamorro MF, Passler T, Bayne J, Stockler J, Woolums AR

AUBURN UNIVERSITY
COLLEGE OF
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Hypothesis

1 .Colostrum-derived BRSV IgG1 titers in nasal secretions (NS) and BALF will be higher and persist longer in dairy calves fed maternal colostrum compared with calves fed a colostrum replacement at birth

2. Colostrum-derived NS and BALF BRSV IgG1 will decay faster compared with BRSV serum neutralizing antibody titers independently of treatment group.

Objectives

1. To determine the transfer and decay of colostrum-derived BRSV IgG1 in NS and BALF of dairy calves fed maternal colostrum or a colostrum replacement.

2. To determine the transfer and decay of colostrum-derived BRSV serum neutralizing antibody (SNA) titers of dairy calves fed maternal colostrum or a colostrum replacement.

3. To compare differences in the persistence of nasal and BALF BRSV IgG1 and BRSV SNA in dairy calves fed maternal colostrum or a colostrum replacement at birth.

45 heifer and bull calves

- AU CVM - Dairy Herd
- **Colostrum replacement: Bovine IgG®**
  - **200 g of Bovine IgG® within first 2h of life**

CR1 group (n=15)

300 g of IgG within 6h of life

- **150 g within first 2h**
- **150 g at 4-6h**

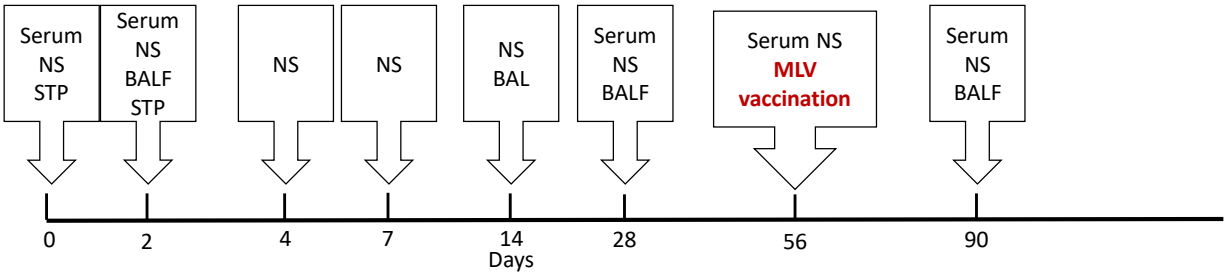
CR2 group (n=15)

300 g of IgG **within 2h of life**

MC group (n=15)

6 L of >22% Brix Maternal Colostrum

- **4 L within first 2h**
- **2 L at 4-6h**

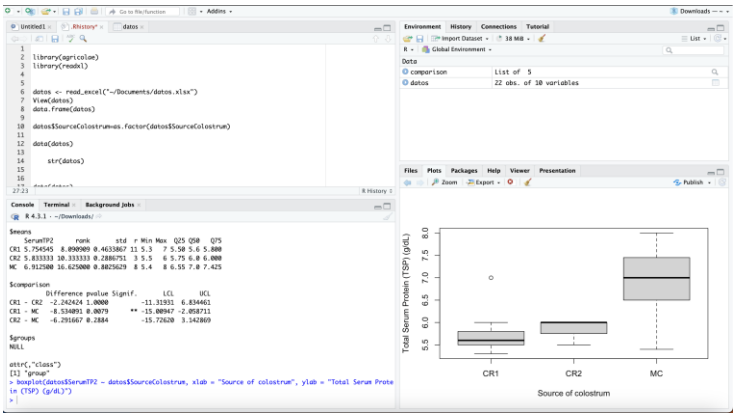


Serum: STP; IgG1 levels; BRSV-SNA titers

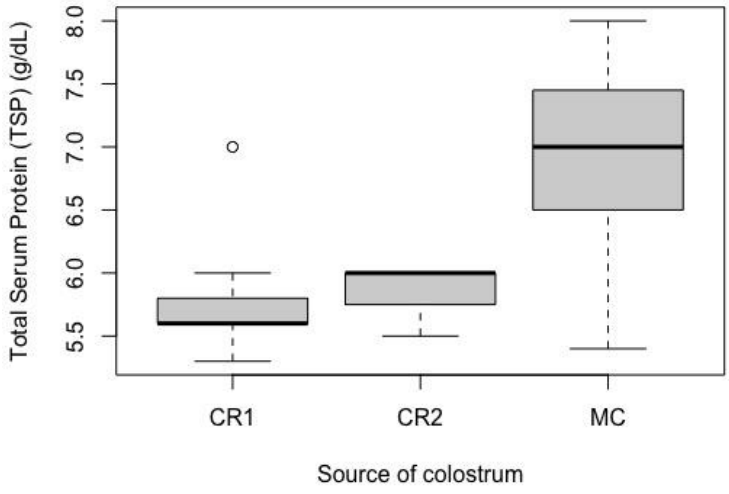
NS: BRSV-IgG1

BALF: BRSV-IgG1

- **Statistical Analysis:**
  - Rstudio
    - Agricolae package
      - Parametric: ANOVA
      - Nonparametric: Kruskal-Wallis
    - EpiR
      - Binomial logistic regression



STP Results

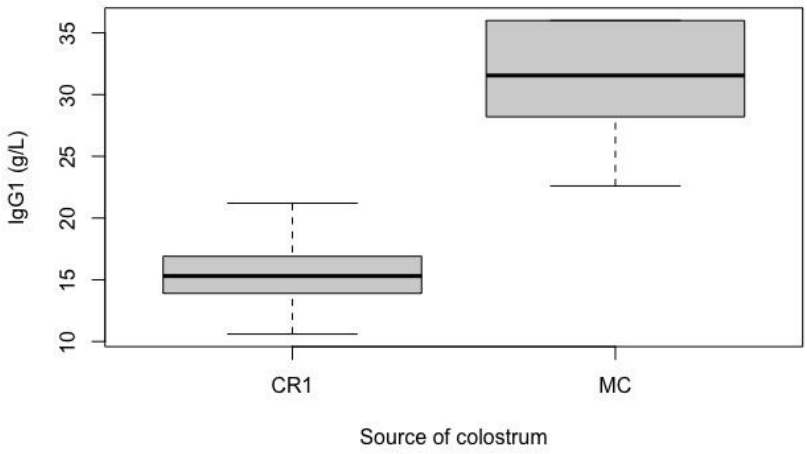


Results

Source of colostrum	n	Mean (mg/dL)	Median	Standard Deviation	Max	Min
CR1	11	5.77	5.8	0.45	7	5.3
CR2	3	5.83	6	0.29	6	5.5
MC	8	6.91	6	0.8	8	5.4

Source of colostrum	Difference	p-value
CR1 vs. CR2	-1.772	1
CR1 vs. MC	-8.335	0.01
CR2 vs. MC	-6.562	0.259

48-hours Serum IgG



48 hours Serum IgG Results

Source of colostrum	n	Mean (gr/L)	Median	Standard Deviation	Max	Min
CR1	11	15.5	15.3	3.07	21.2	10.6
MC	8	30.98	31.5	5.1	36	22.6

Source of colostrum	Difference	p-value
CR1 vs. MC	-7	1e-0

Brix of Colostrum Replacer

Source of colostrum	n	1ST Bag (150 gr IgG)	2nd Bag (150 gr IgG)
CR1	2	28.85	29.4
CR2	4	28.67	28.5

Serum IgG g/L (SD)

Group	Serum IgG 0h	Serum IgG 48h	AEA (%)
CR 1	1.3 (1.4) [a]	15.3 ***a**	14.3 [a]
CR 2	0.4 (0.6) [a]	15.6 ***a**	15.1 [a]
MC	1 (0.9) [a]	31.4 ***b**	N/A

*p<0.05 within group
Different letters in columns = p<0.05 between groups

Categories of IgG (g/L) transfer

Group	Excellent (> 25)	Good (18 - 24.9)	Fair (10-17.9 24)	Failure (< 10)
CR1	0	1/11	10/11	0
CR2	0	1/7	6/7	0
MC	8/9	1/9	0	0

Discussion

- The mean STP of calves fed with CR >5.5 g/dL is correlated with adequate transfer of passive immunity in dairy calves
- A greater IgG mass delivered in 4 L of MC and timing (150 g IgG at 2h and 150 g of IgG at 6h) could have resulted in reduction of IgG efficiency of absorption and explain lower IgG values in CR1 calves

- 6 L of high quality (>22% Brix) MC within 6h of birth results in serum IgG levels above the standard recommendation for Excellent transfer of passive immunity in dairy calves
- 300 g of IgG from a CR within 6h of birth may result in different levels of serum IgG depending on the protocol/frequency of administration
- The lower STP levels in calves fed CR are the result of protein alteration during manufacturing process

- 300 g of IgG from the colostrum replacer product used in this study do not result in excellent transfer of passive immunity in dairy calves based on the recommendations from the new standards of passive immunity
- A greater non-IgG solids/IgG ratio in the colostrum replacer could have negatively affected IgG absorption in CR1 and CR2 groups
- A greater total IgG mass fed in 6 L of maternal colostrum within 12 hours of life could have resulted in greater serum IgG levels in MC calves

Acknowledgments

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Thank you.

Questions?