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Research Article

Effect of Periparturient Intranasal Vaccination on Post Parturient Health Parameters in Holstein Cows

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Abstract

The objective of this study was to evaluate the effect on health and reproductive performance of vaccinating Holstein cows with an intranasal modified live viral vaccine (INV) during the peri-parturient period. Two conventional, free stall dairies and one organic certified dairy were enrolled in the study. In the two conventional dairies cows were vaccinated 18-24 days prior to expected parturition. In the third herd cows were vaccinated 18-24 days prior to expected calving date, within twelve hours after parturition or at both time points. Cattle were blocked based on parity group and expected calving date and randomized to the experimental treatments (vaccination and control) within blocks. Health and reproductive outcomes were monitored and compared to matched, randomly assigned control cows. Results from the first two dairies were used to determine power calculations for the final study in herd 3. Th incorporation of an intranasal viral vaccine program decreased the total cows removed from the herd throughout the lactation, decreased presentation of retained fetal membranes, and lower incidences of pneumonia and mastits. Overall, a greater impact was determined with two doses and, if one dose was administered, the results tended to favor administration at calving.

Keywords: postpartum health, postpartum immune suppression, calving stress, intranasal vaccination, immunomodulation

Abbreviations: RFM: Retained Fetal Membranes; BRSV: Bovine Respiratory Syncytial Virus; CON: Non-Vaccinated Negative Control; AI: Artificial Insemination

Introduction

The transition period is a critical time for cow health, survival, and subsequent fertility. While some of the post-partum diseases are more nutritional in cause (hypocalcemia, ketosis, displaced abomasum), others have more of an immunological/infectious underlying cause (retained fetal membranes [RFM], uterine infections, and pneumonia). Incidences of these diseases and their multifactorial nature have been described in detail [1,2] and a more recent study by McNeel [3] demonstrated that there is also a genetic component to most postpartum health disorders.

In addition to hormonal and nutritional changes, and associated with those factors, cows going through the transition period display pronounced systemic immune suppression [4]. Immunosuppression in periparturient dairy cows has been well documented and specific dysfunction of both lymphocytes and neutrophils in both periparturient cows and sows, has been demonstrated [5-7]. This suppression of the immune system has been associated with increased susceptibility to infectious diseases in many systems including respiratory, reproductive and gastrointestinal organs [8-12].

While increased immune suppression can be determined beginning three weeks prepartum [13,14], broad immune suppression is more dramatic in the first two weeks postpartum

[15-23]. While the exact causes of immune suppression in these animals are not clear, hormonal and metabolic changes are thought to influence the reduction seen in systemic immune responses.

Little research has characterized the mucosal respiratory immune response of adult cattle in the peripartum period. However, a recent study by Cortese [24] showed that both antigen specific and antigen nonspecific nasal immune responses of mature dairy cows following intranasal administration of a modified live viral vaccine [bovine respiratory syncytial virus , bovine herpesvirus -1 and parainfluenza virus type 3; Inforce 3, Zoetis, (INV)] was higher in cows vaccinated on the day of calving than in cows receiving the vaccine 2-3 weeks prior to calving. Consequently, this study examined the health and reproductive performance of cows administered intranasal modified live viral vaccine during the periparturient period when compared to unvaccinated controls in three U.S. dairy herds.

Materials and Methods

Study population

This study was conducted using a randomized complete block experimental design. Pregnant Holstein cows were eligible for enrollment and the blocking criteria included parity grouping and expected calving date. Each block consisted of two (studies 1 and 2) or four (study 3) treatment groups and animals were randomly assigned to cows within a block.

Treatment protocol in Dairies 1 and Dairy 2

Table 1: Distribution of cows by study location, treatment, and parity category*.

	Location Number		
Group	1*	≥2	Total
Dairy 1			
Control	182	292	485
INV**	193	287	469
Total	954		
Dairy 2			
Control	216	405	621
INV**	201	396	597
Total	1218		
Dairy 3			
Control		1245	1245
INV***		3589	3589
Total	4834		

*First parity cows were heifers at time of INV administration, parity ≥2 cows were in the dry period after completing their prior lactation.

**Intranasal vaccine (INV) administered 14-21 days pre-calving (PC)

***see Table 2.

Dairy 1 (D1) and dairy 2 (D2) were conventional free-stall dairies located in the Northeast (D1) and the Midwest (D2). Cow information was obtained from on-farm software and animals were blocked by parity and expected calving date and then randomly assigned into 1 of 2 treatment groups: 1) non-vaccinated negative control (CON); or 2) intranasal vaccination before calving (PC). Individual enrollments occurred when cows were moved to the close-up pens 3 weeks before expected calving date and the treatments were administered 18-24 days before expected calving date. Separated close-up pens with headlocks were used to house CON or PC cows. Pens for each treatment group were on opposite sides of a central feed delivery alley and were separated by approximately 20 feet of free air space to prevent nose to nose contact and cross-contamination of feed, and water, and was intended to prevent drift of aerosolized vaccine from vaccinates to CON cows. No direct inter-treatment contact was allowed for a minimum of 2 weeks post-treatment. Halfway through the study pens were switched for each group. Cows that calved less than seven days after treatment administration were excluded from the statistical analysis. All the health events were recorded in a commercial dairy software program (Dairy Comp 305). Animal numbers are displayed in Table 1.

Treatment protocol in Dairy 3

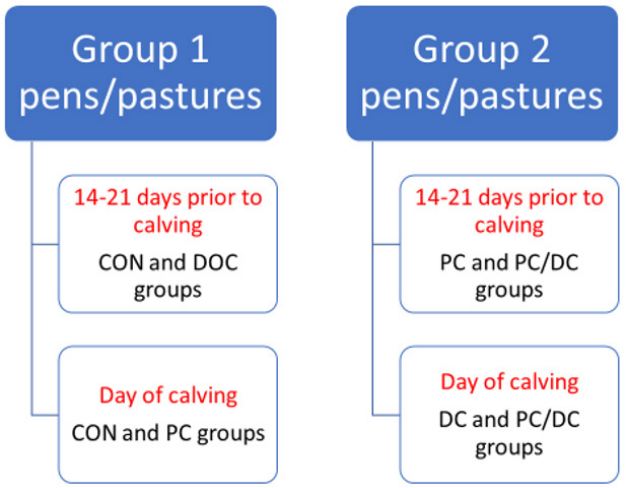

Figure 1: Cow movement/pen-pasture assignment for Dairy 3 study.

Dairy three (D3) was a large, organic certified dairy located in the Southwest (Table 1). Only cows that had completed at least one lactation were included in the study. Based on Cortese et al. (2017), three vaccination groups were considered in this location. Animals were individually identified and blocked by parity and expected calving date and randomly assigned into 1 of 4 treatment groups: 1) non-vaccinated negative control (CON); 2) intranasal vaccination at 18-24 days prior to calving (PC); 3) intranasal vaccination at the day of calving within twelve hours of parturition (DC); or 4) intranasal vaccination at both 18-24 days prior to calving and at the day of calving (PC/DC; Table 2). Once treatments were administered, the groups were separated to avoid nose-to-nose, feed, and water contact, and a minimum of 25 feet of free air space was maintained between pens/pastures for 2 weeks post-vaccination to avoid potential cross vaccination among groups. This requirement

allowed for two groups to be housed together at each vaccination point: Negative control and cows vaccinated at calving were able to be housed together as could cows vaccinated pre-partum with those vaccinated prepartum and at calving until vaccination were administered at calving (Figure 1). Cow records were maintained on a commercial dairy software system (PC Dart).

Table 2: Distribution of cows across treatments for dairy 3.

Parity Group	Vaccination Program	Vaccines Given	No. Animals	Vaccination Timing
≥2	Control	None	1245	NA
≥2	INV PC	INV	1198	18-24d pre-partum (a)
≥2	INV DC	INV	1250	Within 12h of calving (b)
≥2	INV PC/DC	INV	1141	a and b

Vaccine administration

Experimental vaccination programs were administered while cows were in the close-up pen and/or at the day of calving. The intranasal vaccine utilized in this study contained modified live bovine respiratory syncytial virus (BRSV), modified live, temperature sensitive bovine herpesvirus -1 (BHV-1) and modified live, temperature sensitive parainfluenza virus type 3 (PI3 V; Inforce 3, Zoetis). The vaccine was administered according to label directions with 2mL in one nostril with cannulas provided by the manufacturer. All vaccines were administered by, or under the supervision of a veterinarian. In dairies 1 and 2, vaccination was administered 18-24 days prior to calving. On D3, vaccination as administered 18-24 days prior to calving, on the day of calving (within 12 hours of giving birth) or at both timepoints.

Routine vaccination programs in the study dairies

Vaccines routinely used by the dairies were continued. Dairy 1 vaccinated cows according to the following program: At approximately 60 days prior to calving, all cows were vaccinated a viral/bacterin scours vaccine and a core *E. coli* mastitis bacterin. Eighteen -24 days prior to calving all cows received a core *E. coli* mastitis bacterin. Heifers were also administered a viral/bacteria scours vaccine.

Dairy 2 utilized the following vaccines administered to all cows: At approximately 60 days prior to calving cows received a *Mannheimia haemolytica* bacterin-luekotoxoid, an autogenous *Salmonella* core bacterin, and a core *E. coli* mastitis bacterin. Eighteen to twenty-four days prior to calving an autogenous *Salmonella* core bacterin, a viral/bacterin scours vaccine and a core *E. coli* mastitis bacterin were administered. At approximately 21 days in milk a modified live 5-way viral vaccine in combination with a five-way *leptospira* vaccine, *Mannheimia haemolytica* bacterin-luekotoxoid and a core *E. coli* mastitis bacterin were administered. At approximately 200 days of pregnancy cows were vaccinated with a modified live 5-way viral vaccine in combination with a 5-way *Leptospira* vaccine and an autogenous *Salmonella* core bacterin.

Dairy 3 vaccination program included a modified live 5-way viral vaccine in combination with a 5-way *leptospira* vaccine and a core *E. coli* mastitis bacterin administered 23-29 days in milk, and a 5-way *leptospira* vaccine at pregnancy diagnosis. At approximately 60 days prior to calving, all cows were vaccinated a viral/bacterin scours vaccine, an 8-way clostridial vaccine and a core *E. coli* mastitis bacterin. Eighteen -24 days prior to calving all cows received a core *E. coli* mastitis bacterin.

Breeding programs

Both D1 and D2 utilized timed artificial insemination (AI) programs. Dairy one was on a presynch, ovsynch program that included a single dose of a prostaglandin with a resynch program on open cows. Dairy 2 applied a double ovsynch program for the first service followed by an ovsynch program with pedometer-based selection on successive breeding. Cows in D3 were subject to a reproductive program based on AI following visual estrus detection. Cows' tail heads were painted daily with color chalk and checked for estrus by removal of tail chalk. If estrus was determined, cows were inseminated during the morning. None of the cows were subjected to any type of estrus or ovulation synchronization protocol. Cows with more than 5 AI or more than 180 days in milk DIM were moved to a pen with a clean-up bull. The Voluntary waiting period was 45 d and pregnancy was diagnosed by transrectal palpation at 60 d after AI.

Statistical analysis

Following enrollment and experimental treatment administration, complete records for each cow were maintained in Dairy Comp 305 or PCDART. Data regarding lactation performance, reproductive events, disease occurrence, mortality, therapeutic treatments and cows sold or that died were collected for each enrolled cow until they either left the herd or completed the lactation. For dairies 1 and 2 mastitis cases were defined as: 1. an initial case in the cow and 2. reoccurrence in the same quarter or a different quarter >7 days from the initial case. For dairy 3 mastitis cases were defined as: 1. an initial case in the cow and 2. reoccurrence in the same quarter or a different quarter >14 days from the initial case. There was no attempt to mask farm personnel regarding experimental treatments assigned to each cow. Since all observations were observed on individual cows, animal was the experimental unit. The model for all traits included the fixed effect of experimental treatment, age, and their interaction and the random effect of month of freshening. The PROC MIXED procedure of SAS was utilized to evaluate continuous data such as 305ME and test day milk yields and log-transformed somatic cell counts. Sums of squares were partitioned to assess effects due to the random effect of block (defined as the month/year the animal freshened) and the fixed effects of treatment group, parity group, and the parity group by treatment interaction. For these analyses a covariate was included that adjusted treatment least squares means based on the potential of each animal to produce milk. Variables used in this regard were either PTA for milk (springing heifers), or 305 ME deviations for each cow within the herd (cows with a lactation

record). In the case where treatment means were computed based on repeated observations (e.g., mean milk yield over 43 weeks based on weekly milk yields), the effect of week of lactation was added to the model as a fixed effect, as was a three-way interaction of treatment by lactation by week Figure 2.

Results

Cow Survival

Table 3 presents the frequencies of cows that left the herd within the first sixty days of lactation and throughout the entire lactation by dairy and vaccination group. In two of the three dairies (D2 and D3), decreases, in total cow removal throughout the lactation, were seen with periparturient vaccination. While not significant, the greatest treatment effect was seen in D2 (4%, P = .12). In D3 vaccination during the peri-parturient period significantly decreased the total cows that were culled and died from 22.1% to 19.4% (P = 0.05) during the lactation following vaccination. A significant reduction in total cows that died during the lactation was determined with any INV schedule (P = 0.028), with the group that received INV on the day of calving having the lowest death loss. Also, the number of cows culled was lowest for PC/DC, followed by cows that received at least one INV dose and highest for the negative control group (P < 0.11). While not significant, the number of cows culled in first 60 days in milk, the total number of cows sold, and the total number of cows sold and died improved if the INV vaccination was administered and improved as vaccination was moved to day of calving and with two doses (Figure 2). There was a 2.9% decrease in total cows removed from the dairy and a 3.7% decrease in total cows culled from the herd if INV was administered twice Table 4.

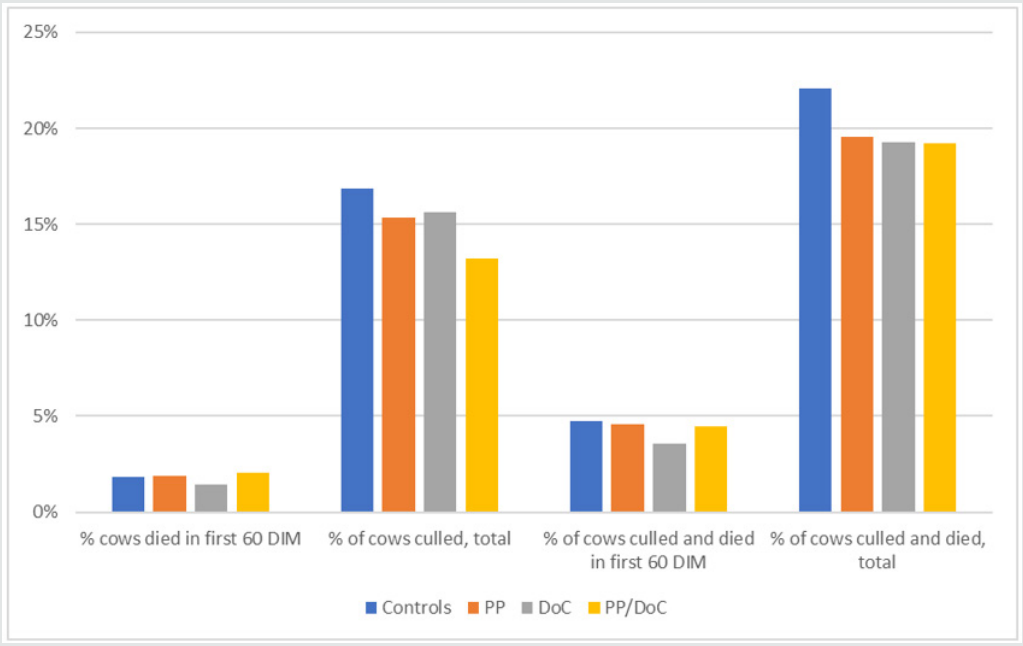

Figure 2: Percentage of cows culled and/or died in first 60 days in milk or total lactation.

Table 3: Effect of vaccination on cow survival by study location.

	60 DIM		Complete lactation	
Group	**Dead and sold**	**P-value**	**Dead and sold cows**	**P-value**
Dairy 1				
Control, %	6.1±1.3	0.85	27.4± 2.4	0.43
INV*, %	6.5±1.2		30.0± 2.3	
Dairy 2				
Control, %	4.6±1.1	0.43	21.6± 2.6	0.12
INV*, %	3.7±1.3		17.6± 2.4	
Dairy 3				
Control, %	4.72	0.72	22.09	0.05
INV**, %	4.23		19.4	

*Intranasal vaccine administered 14-21 days pre-calving (PC)

**All three vaccinate groups included in summary analysis of dairy 3.

Table 4: Cow removal from dairy three by vaccination group.

	Experimental Treatment Group[1]			
Item	CON	PC	DC	PC/DC
No. cows	1245	1198	1250	1141
Percentage of cows died and sold in first 60 DIM	4.7±0.7	4.6±0.7	3.6±0.6	4.4±0.7
Percentage of cows died and sold, total lactation	22.1±2.6	19.6±2.4	19.3±2.3	19.2±2.4

[1]CON = negative control; PC = 21-days prepartum; DC = at calving; PC/DC = 21-days prepartum and at calving; treatment effect p-value P < 0.55 for first 60 DIM and P < 0.26 for total lactation

Mastitis

Table 5 shows mastitis incidence by treatment group. Decreases in mastitis, while not significant were seen in both dairy 1 and 2 in the first 60 days of milk and throughout lactation in INV vaccinated cows. In dairy 3, significant differences were detected between treatment groups for percent of cows ($P < 0.014$) and number of mastitis cases ($P < 0.0043$) within the first 60 days in milk and throughout the entire lactation. For each treatment group, the number of cases per 100 cows per lactation was high, indicating that a significant proportion of cows had more than one case of mastitis. The number of cases /100 cows, both in the first 60 days and throughout the lactation, were significantly higher for the CON group. Cows receiving two INV doses had the lowest incidence, followed by cows vaccinated at calving and then cows receiving the 21-day pre-partum dose (Table 6 & Figure 3). When considering the entire lactation, the same general trend occurred with the negative control group having the greatest number of cows with at least one case of mastitis, the twice dosed treatment group had the fewest number of cows and the single dose groups was in between (P < 0.10). When considering the number of cases across the entire lactation, there was a significant treatment effect with twice dosed cows having the fewest cases per 100 cows (86.5) and the negative controls (99.8) and cows vaccinated at calving (99.9) then highest (P < 0.0049) (Figure 3).

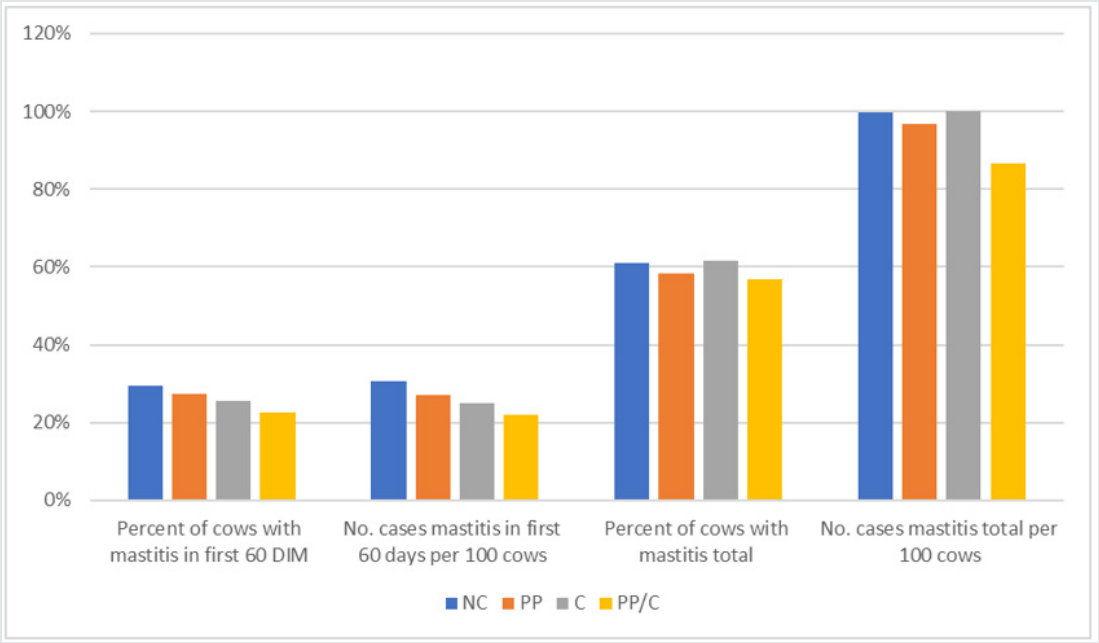

Figure 3: Mastitis incidence in the first 60 days and complete lactation.

Table 5: Effect of vaccination on incidence of clinical mastitis.

	60 DIM		Complete lactation	
Group	Mastitis cases	P-value	Mastitis cases	P-value
Dairy 1				
Control, %	16.0±3.8	0.41	85.6± 12.6	0.71
INV*, %	14.0±3.8		82.9± 82.9	
Dairy 2				
Control, %	15.4±1.7	0.41	54.6±3.8	0.26
INV*, %	13.4±1.7		49.6±3.9	

Dairy 3				
Control, %	29.5	0.26	60.9±5.5	0.27
INV**, %	25.3		58.3±5.7	

*Intranasal vaccine (INV) administered 14-21 days pre-calving (PC)

**All three vaccinate groups included in summary analysis of dairy 3.

Table 6: Mastitis incidence in dairy 3 by treatment group.

Item	Experimental Treatment Group[1]				P-value[2]
	CON	PC	DC	PC/DC	
No. cows	1245	1198	1250	1141	
Cows with mastitis first 60 DIM, % (n)	29.40% (-262)	27.40% (-235)	25.50% (-243)	22.60% (-188)	0.014
Mastitis cases first 60 DIM per 100 cows, % (n)	30.5 (-306)	27 (-264)	27 (-264)	21.9 (-205)	0.0043

[1]CON = negative control; PC = 21-days prepartum; DC = at calving; PC/C = 21-days prepartum and at calving

2For percent cows with mastitis first 60 days, PC/C differed from CON ($P < 0.0018$) and PC ($P < 0.0265$) and DC differed from CON ($P < 0.0688$); for number cases mastitis first 60 days, PC/C differed from CON ($P < 0.0004$) and PC ($P < 0.0296$) and DC differed from CON ($P < 0.0277$); for percent cows with mastitis total, PC/C differed from CON ($P < 0.060$) and DC ($P < 0.0301$); and for number of total cases mastitis, PC/C differed from CON ($P < 0.0017$), DC ($P < 0.0015$) and PC ($P < 0.0167$).

Table 7: Incidence of reproductive health disorders in all three dairies. this is incorrect title.

Group	Retained Fetal Membranes	P-value	Metritis	P-value
Dairy 1				
Control, %	3.9±1.4	0.04	8.7±3.8	0.06
INV*, %	1.4±0.7		5.5±2.5	
Dairy 2				
Control, %	11±1.2	0.2	9.0±1.3	0.33
INV**, %	8.8±1.1		7.4±12	
Dairy 3				
Control1, %	0.55±0.23	**	27.6	0.22
INV**, %	0.35±0.29		25.4	

*Intranasal vaccine administered 14-21 days pre-calving (PC).

[1]Number of retained fetal membranes too low for statistical analysis).

**All three vaccinate groups included in summary analysis of dairy 3.

Postpartum Reproductive Health

The frequency of reproductive disorders was lower for vaccinated cows in D1. While the number of RFM decreased with INV vaccination in D3, the extremely low number of RFM in this herd made statistical evaluation impossible. Dairy 3 metritis levels were high enough for evaluation; however, while INV vaccination decreased the percent of uterine infection by over 2%, there was no statistical difference. Figure 4 shows the impact on incidence of metritis and RFM by vaccination group for D3 (Table 8).

Table 8: Impact of vaccination on reproductive health disorders by vaccination group- dairy 3.

	Experimental Treatment Group[1]				
Item	CON	PC	C	PC/C	P-value
No. cows	1245	1198	1250	1141	
Cases of retained fetal membranes per 100 cows (%?)	0.55	0.79	0.00003	0.000001	*
Cases of metritis per 100 cows, % (n)	2.3 (25)	2.6 (25)	1.8 (21)	1.4 (21)	0.43
Cases of endometritis per 100 cows, %(n)	14.1 (162)	14.4 (158)	13.1 (154)	13.7 (149)	0.92

Cases of pyometra per 100 cows, % (n)	10.7 (119)	9.3 (94)	7.9 (85)	9.4 (89)	0.22
Cases of metritis, endometritis and pyometra combined per 100 cows, % (n)	27.7 (306)	26.8 (277)	23.6 (260)	26.1 (259)	0.31

1CON = negative control; PC = 21-days prepartum; DC = at calving; PC/C = 21-days prepartum and at calving
*Number of retained fetal membranes too low for statistical analysis.

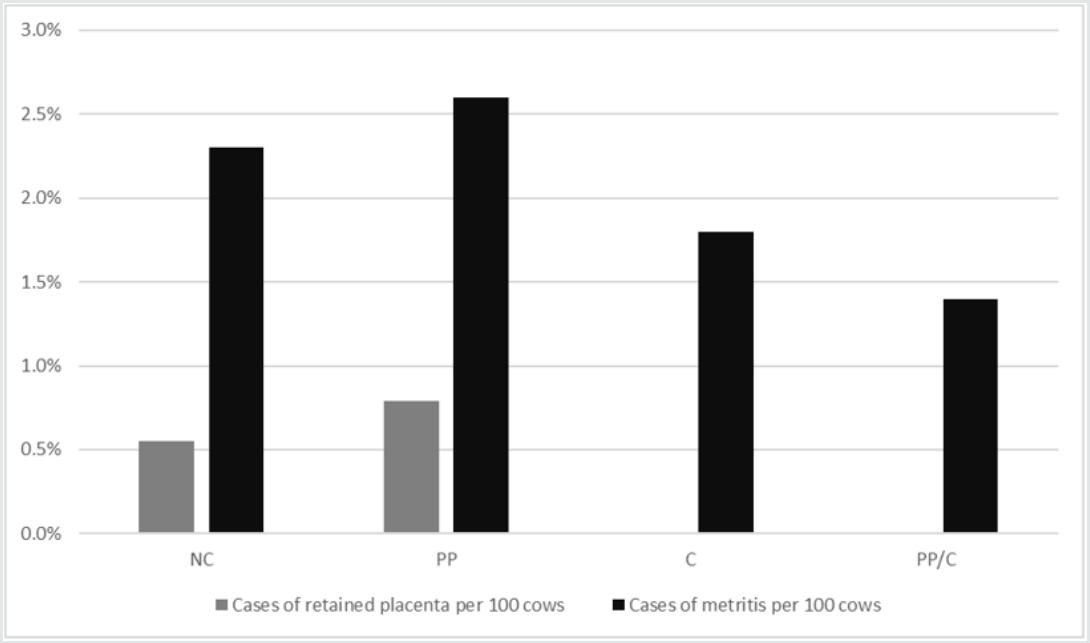

Figure 4: Impact of vaccination on reproductive health disorders by vaccination group- dairy 3.

Post-Partum Pneumonia and other Health Disorders

Cows vaccinated in D3 exhibited decreases in pneumonia that were only significant when evaluated throughout the entire lactation (Table 9). While not significant, some reduction in the incidence of pneumonia was determined in D1. It is interesting to note, that while not significant, D2 had a higher level of pneumonia in the vaccinates. Figure 5 shows the incidence of pneumonia by vaccination group for dairy 3. Treatment comparisons for other health disorders for D3 are shown in Table 10. Most of the health events were at relatively low frequencies with no differences between treatment groups in all three dairies. One exception to this was the incidence rate of lameness in D3. While not significant (*P* = 0.09), vaccinated cows trended toward lower levels of lameness.

Table 9: Impact of vaccination on incidence of pneumonia by dairy.

Group	60 DIM		Complete lactation	
	Pneumonia per 100cows	P-value	Pneumonia Pneumonia	P-value
Dairy 1				
Control, n	2.4±1.1	0.32	5	0.93
INV*, n	1.3±1.1		4.9	
Dairy 2				
Control, n	7.9±1.6	0.46	10.0±1.4	0.44
INV*, n	9.1±1.8		11.4±1.6	
Dairy 3				
Control, n	3.9±1.4	0..09	7.6±1.9	0.06
INV**, n	2.4±1.0		5.7±1.4	

*Intranasal vaccine administered 14-21 days pre-calving (PC).

**All three vaccinate groups included in summary analysis of dairy 3.

Table 10: Dairy 3 summary of other health events incidence rates by vaccination group.

	Experimental Treatment Group1				
Item	**CON**	**PC**	**C**	**PC/C**	**P-value**
No. cows	1245	1198	1250	1141	
Cases of hypocalcemia per 100 cows	1.99	2.13	1.35	1.63	0.53
Cases of ketosis per 100 cows	5.1	5.2	5.7	4.8	0.78
Cases of digestive disorders per 100 cows	5.1	5.2	6.0	6.0	0.77
Cases of other health related issues per 100 cows	12.7	10.7	11.1	13.2	0.25
Cases of displaced abomasum per 100 cows	0.46	1.22	1.38	0.91	0.29
Cases of lameness per 100 cows	30.6	24.5	27.1	28.4	0.09

[1]CON = negative control; PC = 21-days prepartum; DC = at calving; PC/C = 21-days prepartum and at calving.

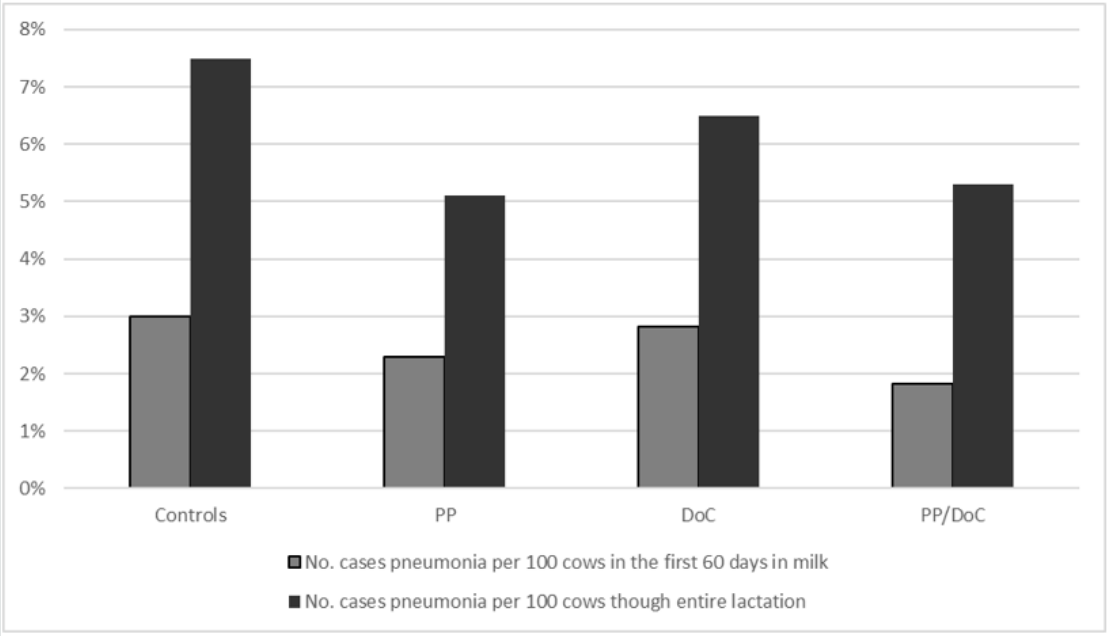

Figure 5: Impact of vaccination on incidence of pneumonia by vaccination group- dairy 3.

Reproductive Performance

Reproductive outcomes for the timed artificial insemination herds and for the herd using estrus detection were analyzed. No differences were seen between the treatment groups.

Milk Production and Milk Quality Parameters

Milk yield and somatic cell count outcomes for D3 are shown in Table 11. Somatic cell count information was not available for dairy 2. It is interesting to note that, despite significant decreases in mastitis, none of the dairies showed an increase in milk production in the vaccinates. In dairy 3, only two variables were significantly different in the yield and somatic cell count variables analyzed. These were test day milk yield in the first and third test days with the group receiving INV at calving having the lowest yields and negative control group the highest yield and the prepartum and twice vaccinated groups in between. Even though differences were detected on these two test days, the difference was not present for either the 2nd, 4th test days and total production.

Table 11: Summary of milk yield and somatic cell count variables – Dairy 3.

	Experimental Treatment Group[1]				
Item	**Negative Control**	**21-d Prepartum**	**Calving**	**21-d Prepartum and Calving**	**P-value**
No. cows	1245	1198	1250	1141	
Lactation records					
Projected 305 ME Milk, lb	21174	21196	21093	21197	0.904
Projected 305 Actual Milk, lb	20860	20897	20835	20890	0.986
Projected 305 ME Fat, lb	799	802	790	788	0.091

Projected 305 Actual Fat, lb	780	783	772	768	0.128
Projected 305 ME Protein, lb	616	615	616	617	0.971
Projected 305 Actual Protein, lb	610	609	610	611	0.984
Lactation average SCC count	3.01	3.07	3.08	2.97	0.164
Test day records					
Test day 1 milk, lb	84.1	83.1	80.7	82.3	P < 0.005[2]
Test day 1 SCC linear score	3.41	3.44	3.5	3.49	P < 0.77
Test day 2 milk, lb	91.4	90.8	90.6	92.2	P < 0.27
Test day 2 SCC linear score	2.79	2.81	2.86	2.78	P < 0.78
Test day 3 milk, lb	86.3	85.3	84.6	85.7	P < 0.014[3]
Test day 3 SCC linear score	2.82	2.85	2.91	2.78	P < 0.485
Test day 4 milk, lb	78.8	79.1	78.5	78.2	P < 0.81
Test day 4 SCC linear score	2.94	2.92	2.94	2.86	P < 0.74

[1]CON = negative control; PC = 21-days prepartum; DC = at calving; PC/C = 21-days prepartum and at calving

[2]For test day 1, DC differed from CON ($P < 0.0005$), PC ($P < 0.0171$) and PC/C ($P < 0.1042$); CON differed from PC/C ($P < 0.0776$).

[3]For test day 3, DC differed from CON ($P < 0.0042$) and PC/C ($P < 0.0417$) and CON differed from PC ($P < 0.0185$).

Discussion and Conclusion

Postpartum health problems and high replacement rates continue to be major issues in the dairy industry. Postpartum health has been shown to impact many aspects of profitability on the dairy including reproduction, and longevity in the herd [25] The causes of post calving health issues are multifactorial involving nutrition, environment and hormonal changes. These changes can lead to metabolic diseases and immunologic dysfunction that can lead to secondary infections. A recent article showed that there is also a genetic coponent to susceptibility to various postpartum problems [3].

Immune modulators have been tested for years to decrease post calving diseases and antibiotic usage by improving the depressed immune system of the postpartum dairy cow. These products have all been administered systemically [26] and have limited success or increased some disease parameters. Most have not passed the research phase to be developed into products to be marketed or have increased some postpartum disorders [26]. However, a recent study suggested that, while the dairy cow is systemically immune suppressed post calving, the local immune system may be spared immune suppression or even up regulated in the postpartum cow [24]. Homing of immune responses bv the local immune system has been well established [27]. Furthermore, studies have demonstrated that the trafficking on the respiratory and reproductive immune system are linked and share common trafficking and upregulation [28]. Intranasal vaccination has also been shown to simulate reproductive tract protection [29] in women. The vaccine, and its components, used in this study have been shown to not only stimulate antigen specific protection but also release of non-specific lymphokines and cytokines that can act as immune modulators [30,31]. Notably, the highest immune response seen when administered on the day of calving [32,33].

The first two studies were intended to examine the impact of the IN vaccine on postpartum pneumonia. The timing of vaccine administration at 18-24 was determined based on the studies indicating that as parturition approaches, immune suppression increases. With the publication of the afore mentioned study indicating potential immune shifting on the day of calving, this group was included in dairy 3. The impact on health outcomes other than pneumonia was unexpected and helped to determine statistical power for the third dairy. Where differences were observed, though not statistically significant across all three dairies, percentage improvement was similar in all three dairies indicating a potential lack of statistical power in the first two dairies. Periparturient vaccination with the INV had a significant impact on lowering RFM and metritis (dairy 1), total cattle removed during the lactation, mastitis in the first 60 DIM and throughout lactation, pneumonia, and lameness. An unexplained increase in ketosis was seen in dairy 2 in the vaccinate group. Outcomes improved as vaccination was moved from 18-24 days prior to calving to the day of calving and generally the best results were seen with the vaccine was administered twice (culls and deads and mastitis outcomes). It is interesting to note that this response was not significant (~.5% decrease in the first 60 days) but the impact on total removals continued to increase during the entire lactation (Table 2).

Collectively, this set of studies indicates that using this INV during the periparturient period improved several postpartum health outcomes due to the up regulation of the immune system and supports earlier work indicating better immune responses when administered on the day of calving [24]. While this vaccine can be used for immune modulation, more importantly this study suggests that future immune modulators may have a better outcome if administered to the local immune system.

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