Experimental and Field Usage of Inactivated BVD or IBR–PI_3–BVD Vaccine in Feedlot Cattle

John A. Schnackel, *D.V.M.*
Fort Dodge Laboratories
Fort Dodge, Iowa 50501

Inactivated bovine viral vaccines were developed as an alternative to modified live virus (MLV) vaccines. Vaccine related reactions have been reported following use of MLV-Bovine Virus Diarrhea (BVD) vaccines.[1] Symptoms reported were anorexia, depression and oculonasal discharge usually occurring 10 to 14 days post vaccination.[2] Mucosal disease symptoms have also been reported.[1] Abortions are a risk with MLV-BVD or IBR vaccines from either vaccination of pregnant animals or from contact with vaccinates. These reactions have not been associated with inactivated vaccines.

Post vaccinal reactions with MLV-BVD vaccines may occur in animals vaccinated while incubating field virus such as those vaccinated in the face of a disease outbreak or those recently exposed. Modified live virus vaccines have a potential of reversion to virulence or contamination with a field virus. Cows infected with BVD virus while pregnant may produce a fetus that carries and sheds BVD virus, but remains serologically negative. It is believed these immunotolerent calves develop mucosal disease lesions following exposure to virulent or attenuated BVD virus.[3]

The activity of the BVD virus is believed to play a significant role in the pathogenesis of bovine respiratory disease. BVD infection in cattle interferes with normal blood clearance of bacteria.[4] This interference may increase the calf's susceptibility to pathogenic bacteria.

MLV-BVD vaccines have been shown to be immunosuppressive. Drs. Kaeberle and Roth, Iowa State University, showed that MLV-BVD vaccine, Singer strain, caused a depression in the number of circulating lymphocytes and in lymphocyte blastogenesis. Neutrophil numbers and function were also depressed.[5] An increase in plasma cortisol levels potentiated the immunosuppressive effects of MLV-BVD vaccine.[6]

Immunosuppression Study

Drs. Kaeberle and Roth of Iowa State University conducted a study of the effects of an inactivated BVD vaccine on the immune system of cattle.[7] Nineteen head of cattle serologically negative for antibodies to BVD and IBR viruses were utilized. The cattle were randomly divided into inactivated BVD*, MLV-BVD** and control groups. Blood samples taken before and after vaccination were used to measure immunologic parameters. These parameters were compared to those of the control animals.

Results:

Primary and secondary immunization with the inactivated BVD virus vaccine had no effect on white cell numbers whereas the MLV-BVD vaccine significantly depressed white cell numbers (Figure 1). The depressed white cells were lymphocytes and neutrophils (Figures 2 and 3).

FIGURE 1

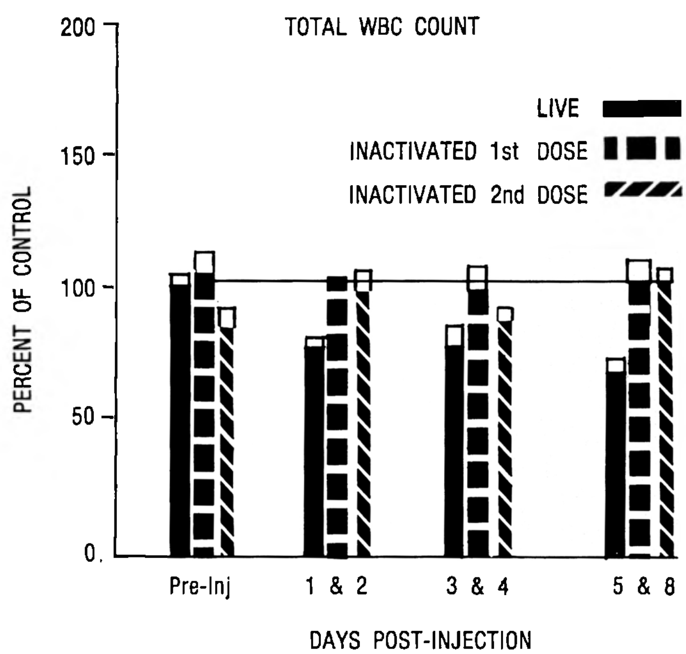

Figure 1: Graph showing mean total white blood cell counts for three groups of experimental cattle compared to the control group pre- and post-vaccination. Open area of each bar indicates the standard error of the mean.

Conclusions:

The MLV-BVD vaccine demonstrated immunosuppressive activity, depressed iodination by neutrophils and altered blastogenic reactivity of lymphocytes. The inactivated virus vaccine did not significantly suppress immunologic function following primary or secondary immunization.

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FIGURE 2

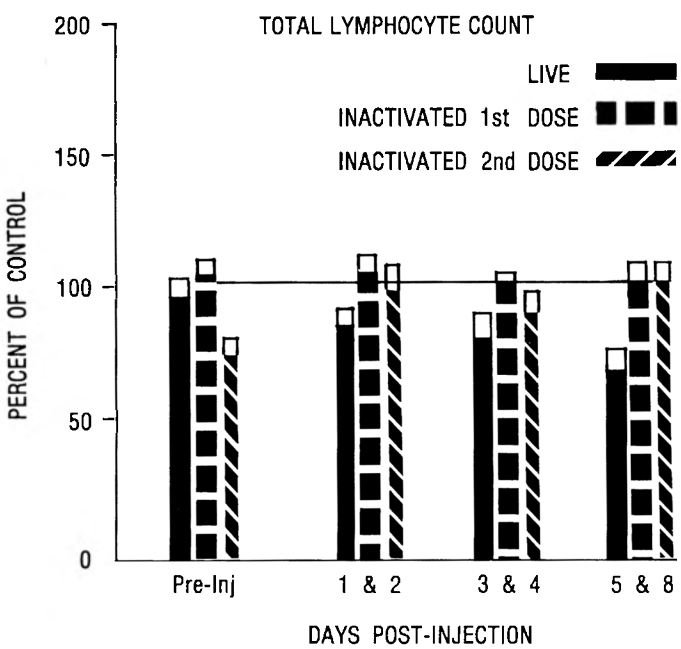

Figure 2: Graph showing mean total blood lymphocyte counts for three groups of experimental cattle compared to the control group pre- and post-vaccination. Open area of each bar indicates the standard error of the mean.

FIGURE 3 TOTAL NEUTROPHIL COUNT

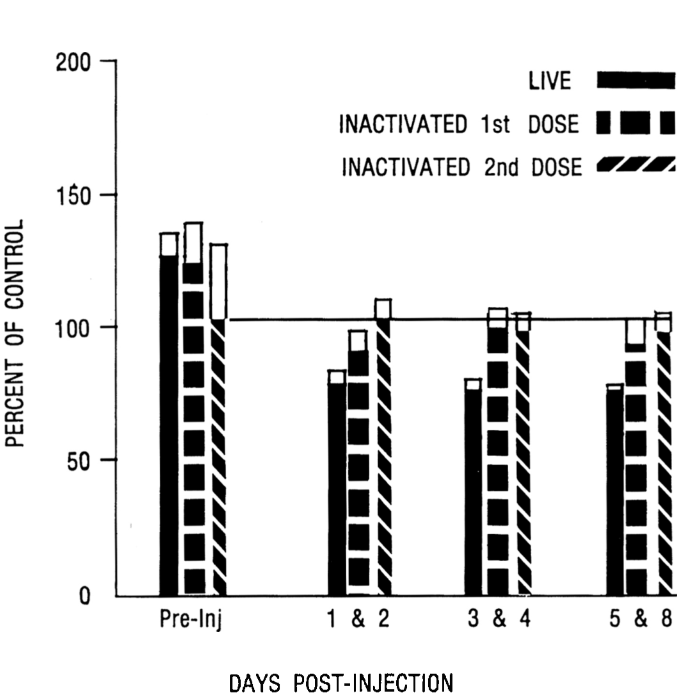

Figure 3: Graph showing mean total blood neutrophil counts for three groups of experimental cattle compared to the control group pre- and post-vaccination. Open area of each bar indicates the standard error of the mean.

Antibody Persistence

Accepted levels of protective antibody are IBR – 1:2, PI_3 – 1:4 and BVD – 1:8. Humoral antibodies in calves vaccinated with inactivated IBR-PI_3 vaccine have persisted for twelve months. A single dose of vaccine twelve months following primary immunization elicited an anamnestic response.[8] (Figure 4) Inactivated BVD vaccine performed in a similar manner. (Figure 5)

FIGURE 4

Vaccination SN Antibody Titers

Number Calves	Pre Vac	2 Wks. Post-Vac	6 Mos. Post-Vac	12 Mos. Post-Vac + Booster	2 Wks. Post Booster
			IBR		
34	<2	49	34	8.6	125
			PI_3		
34	<2	571	134	174	1367
			Controls		
12	<2	ND	<2	<2	<2

N.D. = Not Determined

FIGURE 5

Vaccination SN Antibody Titer

Number Calves	Pre Vac	2 Wks. Post-Vac	6 Mos. Post-Vac	12 Mos. Post-Vac + Booster	2 Wks. Post Booster
			BVD		
20	<2	56	38	23	375
			Controls		
5	<2	<2	<2	<2	<2

Challenge Studies

Ten calves, five vaccinates and five controls, were challenged with the Cooper strain of IBR virus*. The only sign seen in the vaccinated calves was a temperature increase above 104°F. lasting two days. Five control calves in the same study had average temperatures above 104°F. for seven days plus anorexia, depression, cough, nasal discharge, and dyspnea.

Ten calves, five vaccinates and five controls were challenged with New York 1 strain of BVD virus. An average temperature peak of 105.6°F. was seen seven days post challenge in the control group. The vaccinates experienced a temperature peak of 104.1°F. on day eight. Clinical signs produced by the challenge virus were mild in both groups. All five vaccinates showed an anamnestic serological response to challenge by day seven. The control

**Provided by National Veterinary Services Laboratory, Ames, Iowa* calves remained negative for BVD antibody until 14 days post challenge and then responded with a primary serological response. (Figure 6)

FIGURE 6

BVD Challenge SN Titers

Pre-Vac	28 Days Post-Vac Virus Challenge	7 Days Post Challenge	14 Days Post Challenge
	5 Vaccinates		
<2	279	456	23,046
	5 Controls		
<2	<2	<2	60

Case History

Calves owned by the University of Nebraska experienced death loss of six calves—two in January, February and March, 1983. Symptoms seen in these calves were poor weight gain, dull appearance, white frothing from the mouth, severe diarrhea and eventual dehydration. The calves were non-responsive to treatment with oxytetracycline and sulfonamides.

Three animals were submitted to the University of Nebraska Veterinary Diagnostic Laboratory. Histopathologic diagnosis was necrotizing gastroenteritis with lymphoid depletion of visceral lymph nodes. Gross and microscopic lesions of all three calves suggested BVD virus infection. BVD virus was isolated from one calf.

The preceding September, the calves were vaccinated with inactivated IBR, PI_3, BVD vaccine plus other vaccines while still nursing their dams. Three weeks later they received a second dose of inactivated viral vaccines and were weaned. In April, 1983, the calves were revaccinated with inactivated BVD. This herd had experienced a low level of abortion which was undiagnosed. The cows were vaccinated with inactivated BVD vaccine during the fall of 1982.

Some of the calves in the herd remained unthrifty during the summer with a few bouts of fevers and listlessness that required treatment. In September, 1983, blood samples from 92 calves were taken and submitted to Dr. McClurkin at the National Animal Disease Laboratory in Ames, Iowa. The results showed a majority of animals had titers of 1:256 or above. BVD virus was isolated from the blood of the seven individuals with titers of 1:16 or lower. The apparent low serotiters to BVD were due to interference caused by the noncytopathic BVD virus in the serum. (Figure 7)

Two of the individuals positive for virus appeared healthy. The other five calves were unthrifty individuals. Closer checking revealed that the unthrifty individuals and those that died were all out of first calf heifers. Calves from mature cows experienced no similar problems.

Discussion

Speculation is that the cow herd had a mild or inapparent BVD virus infection at a critical time while pregnant with this group of calves. The mature cows had some prior immunity to BVD virus but the first calf heifers were susceptible and became infected with a non-cytopathic strain of BVD virus. Their fetuses' immune systems failed to recognize the virus as foreign, therefore these individuals were born immune tolerant to BVD virus. They were also immunoincompetent to BVD antigen and failed to serologically respond to vaccination. When later exposed to virulent BVD virus, these individuals developed lesions which resulted in chronic infection or death.

FIGURE 7

Blood Test Results

	Number of Animals	Titer
	72	1:256
	8	1:128
	2	1:64
	3	1:32
	BVD Virus Positive	
	1	1:16
	2	1:8
	2	1:4
	2	Negative
Total	92	

North Dakota BVD Vaccination Trial

Personnel at North Dakota State University vaccinated 45 calves with inactivated BVD* vaccine and another 15 with Singer strain MLV-BVD** vaccine. Those that received the MLV vaccine had apparently experienced subclinical BVD infection before entering the study. To get maximum titer, each group required two doses of vaccine. Levels and duration of titers to two doses of inactivated vaccine were greater than to two doses of MLV vaccine. *(Figure 8)*

Field trails to evaluate vaccine performance are difficult to devise because of variables such as stress, disease exposure and previous vaccination. Also, type of cattle, age, breed and weight will affect growth performance. Therefore, results of field trials show trends which may or may not be significant.

Trial 1

This trial was conducted by the Department of Veterinary Extension, Kansas State University, Drs. Homer K. Caley and George Davis. Eighty-six calves were divided into two groups. One group received inactivated IBR-PI_3-BVD vaccine, the other MLV vaccine. There was a slight but not

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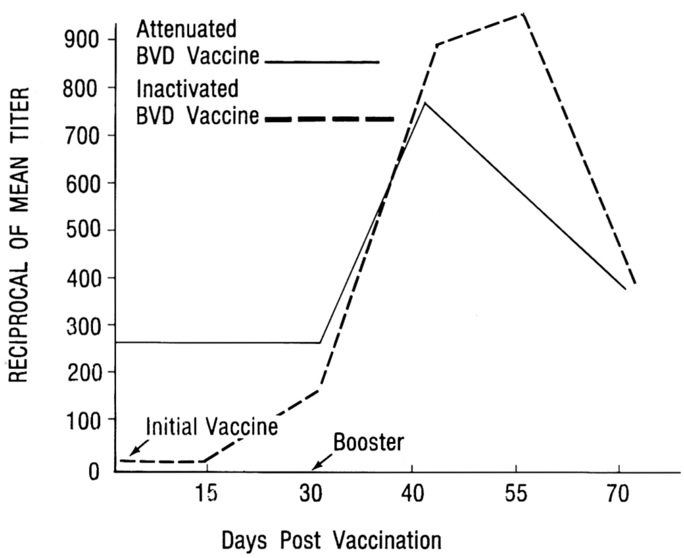
***Attenuated BVD vaccine, Dellen Laboratory, Omaha, Nebraska*

FIGURE 8

North Dakota Trial



significant benefit in weight gain and feed conversion and a 54% reduction in clinical illness in the inactivated vaccine group. (Figure 9)

FIGURE 9

Kansas State University Trial #1

Data	Vaccine MLV-IBR, BVD, PI	Inact.-IBR, BVD, PI
No. Calves	43	43
Avg. Wt. Lbs		
Initial	519.7	511.5
Final (30 days)	593.2	588
Daily Gain	2.65	2.75
Avg. Feed Consumption (dry basis)		
Daily	12.67	12.65
Per Lb. Gain	5.47	4.80
Health		
Sick, No. (%)	13 (30.2)	7 (16.3)
No. Times Treated, Avg.	6.7	6
Deaths	0	0

Trial 2

This trial was also conducted by Kansas State University, Drs. Homer Caley and Mark Spire. Cattle were randomly sorted into two 180 head treatment groups. One group received inactivated BVD vaccine. The other group received NADL strain of attenuated BVD vaccine. The modified live virus vaccine group had a weight gain advantage while the inactivated virus vaccine group had less illness. (Figure 10)

FIGURE 10

Kansas State University Trial #2

Data	Vaccine Treatment Inactivated BVD	MLV BVD
Number	180	180
In weight (lbs.)	564	557
30 Day weight (lbs.)	619	618
Average Daily Gain	1.86	2.03
Sickness (head	1	4
Deaths	0	0

Conclusion

Modified live viral vaccines have been available for approximately twenty years. During that time the use of MLV vaccines have failed to reduce incidence of disease. Both IBR and BVD have increased prevalence within the cattle population.

MLV-BVD vaccines have been associated with post vaccinal reactions and have been shown to be immunosuppressive. Inactivated BVD and IBR-PI_3-BVD have not been associated with post vaccinal reactions and have been shown not to be immunosuppressive.

Research trials have shown that inactivated vaccines will induce an immune response in vaccinated animals and will reduce disease symptoms when those animals are challenged. A disadvantage of inactivated bovine viral vaccines is the need for two initial doses to induce solid primary immunity in seronegative animals. A recent study at Kansas State University concluded that two doses of MLV vaccine were required to get optimum reduction in morbidity and mortality from respiratory disease in feedlot cattle.[9] If this is the case, then inactivated vaccines offer a safe and effective alternative to MLV vaccine for disease control.

References

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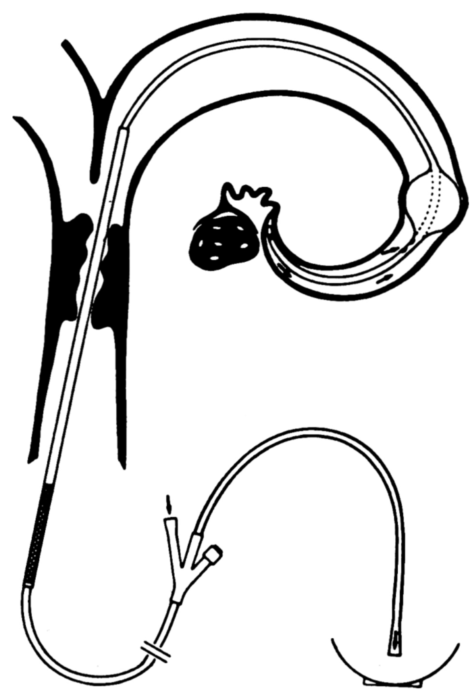

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