Cow Calf - Feedlot Session

Dr. Al Edwards and Dr. Don Hudson, *Presiding*

Effect of Interferon on Feedlot Cattle

Joseph M. Cummins, *D.V.M., PhD.*
David P. Hutcheson, *PhD.*
Texas Agricultural Experiment Station
Texas A & M University
Amarillo, Texas 79106

Summary

There was no significant difference in mortality between vaccinated and control calves. However, vaccination delayed death; the earliest deaths occurred among control calves. Ninety-six calves seronegative for IBR virus antibody were vaccinated and 82 of 86 (95.3%) of the survivors seroconverted within 14 days. Only 2 of 84 surviving control calves developed antibody to IBR virus by 14 days. Most vaccinated calves tested developed intranasal IFN after vaccination. Interferon was detected in many unvaccinated calves without evidence of IBR virus infection. Twenty-seven calves had IFN present in the NS at the time of vaccination. Twenty of these calves survived and seroconverted to IBR virus by 14 days after vaccination. This intranasal vaccine was effective on seronegative cattle with known intranasal IFN titers during a shipping fever outbreak.

Introduction

Interferon (IFN) has been detected in the serum and nasal secretions (NS) of cattle inoculated with infectious bovine rhinotracheitis (IBR) virus.[1-10] Because avirulent IBR virus has been shown to be an effective IFN inducer, and because protection by IFN against heterologous respiratory tract viral infections has been shown,[4,8-10] the present experiment tested the hypothesis that NS-IFN induced by an IBR/para-influenza-3 (PI-3) vaccine would protect calves against natural viral challenge during a shipping fever outbreak.

Materials and Methods

Cell cultures—Bovine fetal kidneys (BFK) obtained at an abattoir were used to prepare BFK cell cultures. Growth and maintenance media for cells consisted of Eagle's minimal essential medium (EMEM) prepared in Hank's balanced salt solution (HBSS) with 10% or 5% bovine fetal serum, respectively, as described.[8]

Viruses—A commercial IBR virus-PI-3 virus vaccine[a] was used to induce IFN. Vesicular stomatitis virus (VSV) was propagated in BFK cells for use in IFN assays.

Assays of interferon—Procedures for the assay of IFN were essentially as described.[11] Before the IFN assay, NS samples were dialyzed overnight in pH 2.0 buffer, dialyzed in phosphate-buffered saline solution of pH 7.2 for 24 additional hours, and some of the samples centrifuged at 108,000 x g for 60 minutes. Nasal secretions were screened for IFN at a 1:20 dilution, and IFN-positive samples were further diluted to determine end points. Interferon titers were expressed as the reciprocals of the dilutions that provided a 50% reduction in the number of VSV plaques as compared with the number in control cultures.

Neutralization tests—Serum antibody titers to IBR virus were determined by microtitration in BFK cells.

Experimental Design—In late January 1981, 201 calves (123 heifers and 78 steers) were assembled by an order buyer from 9 salebarns in Tennessee and South Carolina. The cattle originated from 87 different farms (Table 1). The payweight for the calves ranged from 305 to 560 pounds. The average weight of heifers was 397 pounds and the average weight of steers was 436. Many of the calves were single purchases from single sources, but as many as 13 originated from a single source (Table 2). The calves were divided into two treatment groups. Sixty-one heifers and 39 steers were given an intranasal IBR/PI-3 vaccine and 62 heifers and 39 steers served as unvaccinated controls. After 3 days of assembling and processing, the vaccinates and controls were placed on separate trucks and shipped 1,180 miles to Amarillo, Texas. In Tennessee, the calves were bled, weighed, rectal temperatures recorded, nasal swabs and NS collected (as described[8]), and IBR/PI-3 vaccine administered. Upon arrival in Texas, the calves were all processed (weighed, bled, rectal temperatures recorded, clostridial bacterins administered, and wormed). Nasal swabs and nasal tampons were collected on 100 calves on the day of arrival and from the rest of the calves on the next day. Nasal

[a] *Rhivin, Pitman-Moore, Inc., Washington Crossing, NJ 08560.*

Table 1. Number of cattle purchased, and which later died, per salebarn: Farms of origin.

Salebarn	Calves Purchased	Farms of Origin	Calves Which Died	Farms of Origin of Calves Which Died
TLC	34	18	3	3
UL	42	27	15	12
PLC	46	13	5	4
CCL	49	14	12	8
RLM	4	3	1	1
LW	9	1	--	--
AL	8	6	--	--
SC	3	2	--	--
TOTAL	201	87	36	28

Table 2. Number of calves purchased from individual farms and calf mortality, by type of purchase.

No. of Calves Purchased From Same Farm	No. of Purchases	Total No. of Calves	No. of Deaths	Mortality Rate (%)
1	50	50	12	24
2	18	36	9	25
3	5	15	1	7
4	4	16	6	38
5	2	10	2	20
6	2	12	1	8
7	1	7	2	29
9	1	9	0	0
10	1	10	0	0
11	1	11	1	9
12	1	12	0	0
13	1	13	2	15
TOTAL	87	201	36	

swabs and nasal tampons were collected at various times after arrival. Blood was collected for antibody determination at 14 and 30 days after vaccination.

Upon arrival at the experimental feedlot, half the surviving calves were assigned to 8 pens in which food was available free-choice in bunks, and the other 100 calves were assigned to 8 pens with pinpointers[b] (individual food monitoring devices) in which only one animal could eat at a time.

Illness was assessed in each calf by assigning 2 points for a fever of $\geq$ 104 F and 1 point each for depression, excessive or mucopurulent nasal discharge, and excessive mucopurulent ocular discharge. Depression was monitored by viewing the calves at daybreak; those calves which failed to stand, stretch, or clean themselves compared to penmates were subjectively assigned a point for depression. Only calves with total scores of at least 3 were regarded as ill.

[b] *Universal Identification Systems, Cookeville, TN 38501.*

Results and Discussion

Respiratory tract disease was evident upon arrival and the first death occurred within a few hours. Illness developed in 165 calves in the first two weeks after arrival and 36 calves died in the first month (Tables 3 and 4 show morbidity and mortality of calves by treatment group and by salebarn, respectively). Sixty-seven of 78 steers (86%) and 96 of 123 (78%) of heifers were scored as clinically ill (Table 5).

Table 3. Morbidity and mortality of calves, by treatment group.

Treatment Group	Number Purchased	Number Clinically Ill	Number of Deaths	Case Fatality Rate	Deaths of Total Purchased
Vaccinated heifers	61	50	14	28.0%	23.0%
Control heifers	62	48*	7	14.6	11.3
Vaccinated steers	39	37	6	16.2	15.4
Control steers	39	30	9	30.0	23.1
Total vaccinated	100	87	20	23.0	20.0
Total controls	101	78	16	20.5	15.8

*Two heifers that died before a clinical score was assessed are counted because, presumably, they would have been scored.

Table 4. Morbidity and mortality of calves, by sale barn.

Sale Barn	Vaccinated Heifers	Control Heifers	Vaccinated Steers	Control Steers	Total Vaccinated	Total Controls
UL	5-9-11*	4-12-12	2-9-10	4-8-9	7-20-21	8-18-21
CCL	7-13-13**	1-10-12	2-10-11	2-10-13	9-23-24	3-20-25
TLC	1-8-10	0-8-11	0-6-6	2-6-7	1-14-16	2-14-18
PLC	1-12-16	2-13-18	1-7-7	1-5-5	2-19-23	3-18-23
RLM	0-2-3	--	1-1-1	--	1-3-4	--
SC	0-2-2	0-1-1	0-3-3	--	0-5-5	0-1-1
AL	--	0-2-2	0-1-1	0-1-5	0-1-1	0-3-7
MS	0-2-2	0-1-1	--	--	0-2-2	0-1-1
LW	0-2-4	0-1-5	--	--	0-2-4	0-1-5
TOTAL	14-50-61	7-48-62	6-37-39	9-30-39	20-87-100	16-78-101

*5-9-11 = 5 deaths, 9 morbid, 11 total in group.

**7-13-13 = 7 of the 13 vaccinated heifers purchased from one sale barn died. This represents half of the 14 deaths that occurred in the vaccinated heifer group.

Although the number of calves with clinical illness was nearly equal in pens versus pinpointers (Table 6), the number of deaths was more than twice as high in the pinpointers (Table 7). The case fatality rate of vaccinates in the pinpointers was 33.3% compared to 11.9% of vaccinates in pens. The case fatality rate of controls in the pinpointers was 25% compared to 12.5% of controls in pens (Table 7). The pinpointer introduces more competition for food than the pen, and less aggressive, sick calves apparently did not eat as well in the pinpointers. Sick calves which ate a total of 2.0 pounds or more food during their first 4 days in the feedlot had a better survival rate (only 12% mortality) than those calves eating < 2.0 pounds (53% mortality) (data now shown).

Calves scored clinically ill were given, for 4 days, either antibiotics, antibiotics plus lactobacilli, lactobacilli alone, or no treatment. Doing nothing appeared to be as beneficial as giving antibiotics, antibiotics plus lactobacilli, or lactobacilli alone (Tables 8 and 9).

The serological status to IBR and PI-3 viruses of calves at the time of purchase in Tennessee was determined; 192 calves were seronegative to IBR virus and 116 were seronegative to PI-3 virus. In addition, serology to respiratory syncytial virus (RSV) and bovine viral diarrhea

Table 5. Distribution of illness scores of calves by sex.

	Steers			Heifers		
Clinical Score*	No. of Vaccinates	No. of Controls	Total	No. of Vaccinates	No. of Controls	Total
3 (least severe)	16	8	24	24	27	51
4	15	13	28	24	13	37
5	6	9	15	2	6	8
Total Ill	37	30	67	50	46	96
Total Purchased	39	39	78	61	62	123

*Clinical score = score assessed on depression, nasal and/or ocular discharge, and fever $\geq$ 104 F.

(BVD) virus was determined. At the start of the trial, there were 140 calves seronegative to BVD virus and 171 seronegative to RSV. The vaccinated calves generally responded to the IBR virus portion of the vaccine as 82 of 86 seronegative calves still surviving at 14 days became seropositive to IBR virus (Table 10). Only 2 of 86 seronegative control calves became seropositive by 14 days after processing. Only 13 of 59 (22%) of controls tested and 11 of 53 (21%) of vaccinates tested seroconverted to PI-3 virus by 14 days after vaccination. The PI-3 virus has been isolated from some nasal swabs collected from calves in Tennessee before vaccination.

Interferon was detected in 27% of the NS collected from 53 of 196 (27%) calves in Tennessee. One hundred and one calves were tested within 1 day of their sale and 14% had IFN in their NS. However, 44% of 71 other calves tested 2 days after their sale had IFN in their NS. The IFN was most likely induced by virus, although other IFN inducers might have been responsible. If calves were febrile ($\geq$ 104 F), the chances were that they also had IFN in their NS (Table 10). Interferon activity was detected in most vaccinated calves after vaccination, but was also detected in most control calves tested (Table 11). Eighty-eight of 99 vaccinates and 79 of 97 controls subsequently developed IFN in their NS.

All groups of calves had detectable IFN in their NS before and after processing. Thirty-six calves were never scored clinically ill, but they had as much IFN activity by 7 days after vaccination as calves that were clinically ill and died (Table 12).

Vaccination did not appear to provide an economic

Table 6. Distribution of illness scores of calves, by location in pens or pinpointers.

	Pens		Pinpointers		Total	
Clinical Score*	No. of Vaccinates	No. of Controls	No. of Vaccinates	No. of Controls	No. of Vaccinates	No. of Controls
3	17	14	23	21	40	35
4	21	14	18	12	39	26
5	4	12	4	3	8	15
Total	42	40	45	36	87	76

*Clinical score = score assessed on depression, nasal and/or ocular discharge, and fever $\geq$ 104 F. Note that 8 of 87 (9%) vaccinated calves had a severity of 5, while 15 of 76 (19.7%) of control calves had that same severity clinical score.

advantage in this trial. Vaccinates suffered higher morbidity and mortality (Tables 3, 4, and 6). However, the most severly ill calves (those with a score of 5) occurred in the control group and control calves tended to die sooner than vaccinated calves. During the 7 days after vaccination, 4 controls but only 1 vaccinate died; during the second 7 days, however, 8 controls and 10 vaccinates died (data now shown). The average daily gains and feed efficiencies (feed/gain) were not significantly different at 56 days, but there was an economic advantage to control calves at earlier times.

Virus isolation attempts from the nasal swabs collected during this trial are continuing. Each dead calf had a complete necropsy and a summary of the pathogens isolated at the Texas A&M Veterinary Medical Diagnostic Laboratory is given in Table 13. The BVD virus isolations by the diagnostic lab were all noncytopathic BVD virus confirmed by fluorescent antibody testing. Only a few

Table 7. Morbidity and mortality of calves in pens or pinpointers.

Treatment Group	Location	Number Purchased	Number Clinically Ill	Number of Deaths	Case Fatality Rate	Deaths of Total Purchased
Vaccinated heifers	-Pen	30	23	4	17.4%	13.3%
Vaccinated heifers	-Pinpointer	31	27	10	37.0	32.3
Control heifers	-Pen	29*	24	1*	4.2	3.4
Control heifers	-Pinpointer	31	22	4	18.2	12.9
Vaccinated steers	-Pen	20	19	1	5.3	5.0
Vaccinated steers	-Pinpointer	19	18	5	27.8	26.3
Control steers	-Pen	20	16	4	25.0	20.0
Control steers	-Pinpointer	19	14	5	35.7	26.3
Total vaccinated	-Pen	50	42	5	11.9	10.0
Total vaccinated	-Pinpointer	50	45	15	33.3	30.0
Total controls	-Pen	49	40	5	12.5	10.2
Total controls	-Pinpointer	50	36	9	25.0	18.0

*Two heifers dead within 24 hours of arrival are not counted.

Table 8. Distribution of calves and their treatment for illness.

	Pens		Pinpointers		Total	
Treatment*	No. of Vaccinates	No. of Controls	No. of Vaccinates	No. of Controls	No. of Vaccinates	No. of Controls
Terrimycin-Erythromycin	10	9	11	10	21	19
Terrimycin-Erythromycin Lactobacilli	11	11	12	9	23	20
Lactobacilli only	10	11	11	8	21	19
None	11	9	11	9	22	18
Total	42	40	45	36	87	76

*Treatment = treatment consisted of 4 days of antibiotics, antibiotics plus lactobacilli, lactobacilli alone, or no treatment. Calves designated for no treatment were processed through the chute for 4 consecutive days.

Table 9. Total number or calves treated and retreated for illness.

Original Treatment	Total No. Treated	Deaths	No. Remaining	Retreated*	Deaths of Retreated	Total Deaths**
Terrimycin-Erythromycin	40	3	37	12	4	7
Terrimycin-Erythromycin Lactobacilli	42	6	36	8	1	7
Lactobacilli only	40	7	33	12	2	9
None	40	5	35	6	1	6+
Total	162	21	141	38	8	29

*Retreated = retreatment was Erythromycin and/or Tylosin for 4 consecutive days.

**Total deaths = number of calves given original treatment which died, plus those which died after retreatment.

+Note that the fewest deaths occurred in calves that received no treatment; these untreated calves were processed like the treated cattle, i.e.--they were placed in the chute, weighed, and rectal temperatures were recorded daily.

Table 10. Temperature and interferon before vaccination.

Temperature	Calves Tested	With Interferon
< 104 F	177	40 (23%)
≥ 104 F	19	13 (68%)
TOTAL	196	53 (27%)

lesions consistent with BVD viral disease were observed at necropsy or histopathology. By 14 days after vaccination 49 of 139 calves (35%) tested seroconverted to BVD virus while 100% (114 of 114) seroconverted to RSV.

The use of the pinpointer allowed a comparison of IFN production by calves that were starving versus those eating. Calves were in shipment February 1 and did not have food or water. Thirteen calves failed to eat for 6 or more consecutive days after arrival. Although only a few IFN titers were determined, it appears that IFN production by starving calves was similar to that of eating calves.

Table 11. Number of calves with interferon in the nasal secretions during the first eleven days of the vaccine study.

Treatment Group	Days After Vaccination								
	0*	4	5	6	7	8	9	10	11
Steers-Vaccinated	17/38+	10/12	6/6	16/16	7/8	2/2	--	5/9	--
Heifers-Vaccinated	10/61	--	8/20	15/17	27/27	12/17	1/1	--	4/8
Total Vaccinated	27/99	10/12	14/26	31/33	34/35	14/19	1/1	5/9	4/8
Steers-Controls	13/38	4/10	5/8	9/20	4/7	1/1	--	0/9	--
Heifers-Controls	13/59	--	13/20	13/19	26/28	11/16	1/1	--	2/7
Total Controls	26/97	4/10	18/28	22/39	30/35	12/17	1/1	0/9	2/7

*0 = day of processing in Tennessee.

+Numerator = number with interferon; denominator = number tested.

Table 12. Number of calves with interferon in the nasal secretions after vaccination: Summary of interferon activity in calves that eventually died versus those that were not scored clinically ill.

Treatment Group	Health Status	Days After Vaccination							
		0*	4	5	6	7	8	10	11
Vaccinates	Dead	7/20+	1/1	4/10	7/7	6/6	5/5	--	--
Control	Dead	6/15	1/2	4/7	1/5	2/3	--	0/2	0/2
Total	Dead	13/35	2/3	8/17	8/12	8/9	5/5	0/2	0/2
Vaccinates	Healthy	1/13	--	2/2	4/6	7/7	2/2	0/1	0/1
Control	Healthy	3/22	1/2	5/7	5/9	6/6	3/6	0/3	0/2
Total	Healthy	4/35	1/2	7/9	9/15	13/13	5/8	0/4	0/3

*0 = day of processing in Tennessee.

+Numerator = number with interferon; denominator = number tested.

In this experiment, an attempt to enhance IFN production by vaccination was not beneficial. Vaccination occurred when 27% of the calves already had IFN in their NS. Although there was more morbidity and mortality in vaccinates, the difference was not significant. Interferon in the NS did not significantly hinder an IBR virus antibody response to the vaccine as the geometric mean titer (GMT) of vaccinates with IFN was 13.9, while the GMT of vaccinates without IFN at the time of vaccination was 14.3.

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