Efficacy of Immunization of Feedlot Calves with a Commercial *Haemophilus somnus* Bacterin

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ABSTRACT

Two cohorts, consisting of 10,723 calves total, were identified in this prospective follow-up study to investigate whether immunization of auction market beef calves immediately upon arrival at the feedlot with a commercial *Haemophilus somnus* whole cell killed bacterin would reduce subsequent mortality. In addition to mortality rate, the use of incidence rate of fatal disease is introduced as an effect measure to examine vaccine efficacy in the feedlot. The *Haemophilus somnus* bacterin had no significant effect on the overall crude mortality rate; however, the bacterin appeared to significantly ($p < 0.05$) reduce the incidence rate of fatal disease and the mortality rate during the first two months in the feedlot, when risk of fatal disease onset was highest. Once mortalities likely not associated with hemophilosis (for example, a fractured femoral neck) were removed from the analysis, steer mortality rate, but not heifer mortality rate, was reduced significantly ($p < 0.05$) in the vaccinated group. The attributable percent overall for steers was 17.4%; this suggests that 17.4% of fatal respiratory disease in the unvaccinated steers could have been prevented by vaccination with the *H. somnus* bacterin. Heifer calves demonstrated a significantly ($p < 0.01$) higher incidence rate of fatal disease during the first week than did steer calves, indicating that a different pattern of fatal disease existed for the two sexes. Use of a second vaccination two weeks after arrival did little to decrease mortality risk.

RÉSUMÉ

Cette étude prospective suivie portait sur deux groupes de veaux, qui en totalisaient 10,723, et elle visait à déterminer si l'immunisation de veaux à boeuf achetés aux encans, immédiatement après leur arrivée dans les parcs d'engraissement, avec une bactérine contre *Haemophilus somnus*, réduirait la mortalité subséquente. Les auteurs considérèrent non seulement le taux de mortalité, mais aussi celui de l'incidence de maladies fatales, afin de vérifier de plus près l'efficacité du vaccin précité, dans les parcs d'engraissement. Ils constatèrent qu'il n'influençait pas de façon significative le taux brut global de mortalité; il sembla cependant diminuer de façon appréciable ($p < 0,05$) le taux d'incidence de maladies fatales et de mortalité, au cours des deux mois ultérieurs à l'arrivée dans les parcs d'engraissement, lorsque le risque d'éclosion de maladies fatales est le plus élevé. Après avoir enlevé de l'analyse statistique les mortalités apparemment non attribuables à *H. somnus*, par exemple la fracture de la tête du fémur, le taux de mortalité des bouvillons, mais non celui des femelles, afficha une diminution significative ($p < 0,05$), chez les sujets vaccinés. Comme le pourcentage global attribuable à l'éclosion de maladies fatales atteignit 17,4%, chez ces bouvillons, il semble qu'on aurait pu prévenir 17,4% des maladies respiratoires fatales chez les témoins, si on leur avait administré la bactérine expérimentale. Les génisses affichèrent un taux d'incidence de maladies fatales significativement plus élevé ($p < 0,01$), au cours de leur première semaine dans les parcs d'engraissement, indice d'un profil différent de ces maladies, selon le sexe. Le recours à une deuxième vaccination, deux semaines après l'arrivée des veaux dans les parcs d'engraissement, contribua peu à diminuer le risque de mortalité.

INTRODUCTION

Various syndromes associated with *Haemophilus somnus* infection in beef calves, including thrombotic meningoencephalitis, septicemia, arthritis, respiratory infections and reproductive failure have been reported (1-3). Average mortality losses from *H. somnus* infections are reported to be 1.3% in surveyed herds of greater than 400 animals (4). Isolation of *H. somnus* from pneumonic bovine lungs has led to the suggestion that this bacterium may play an important role in bovine respiratory disease (3,4). *Haemophilus somnus* may therefore be a significant contributor to feedlot mortality, especially as a cause of thrombotic meningoencephalitis and as a component of sufficient cause or causes of bovine respiratory disease (5).

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Feedlot managers in western Canada frequently purchase a majority of their calves from auction markets; the immune status of these calves with respect to *H. somnus* is usually unknown. Feedlot managers and their veterinarians must therefore decide whether vaccination with a *H. somnus* bacterin upon arrival will give a sufficient number of immuno-naive calves enough time to develop immunity so that subsequent morbidity and mortality to hemophilosis are reduced significantly.

A commercial *H. somnus* bacterin became available in September 1978 (6). Few field trials have examined the effectiveness of this bacterin in feedlot conditions; those trials that have report equivocal results. Reporting on the first year of the Bruce County observational study in Ontario the authors noted that using a *H. somnus* bacterin was strongly associated with no or low mortality, although only three feedlots used the bacterin out of a total 66 feedlots in the study (7). The authors concluded that the overall importance of the vaccine was therefore difficult to assess. Similar findings and conclusions were reported for the second and third years of that same study (8,9). No significant reduction in total mortality or number of animals treated for bovine respiratory disease (BRD) could be demonstrated in two prospective field trials (10,11). In a third such trial, single vaccinates had significantly greater BRD morbidity than either controls or double vaccinates (12).

The purpose of this prospective follow-up study was to investigate whether immunization of auction market beef calves immediately upon arrival at the feedlot with a commercial *H. somnus* whole cell killed bacterin would reduce subsequent mortality. In addition, examination of the patterns of disease and determination of the periods of greater risk of hemophilosis using appropriate epidemiological measures were attempted to better understand the dynamics of *H. somnus* bacterin effects.

MATERIALS AND METHODS

THE FEEDLOT

Two cohorts were identified on a large 15,000 head capacity commercial feedlot in southwestern Alberta. This particular feedlot was well suited for a prospective follow-up study of this nature because: (i) a large number of auction market exotic-cross beef calves were fed beginning in September of each year; (ii) calves were individually identified and case records were maintained on each calf in a feedlot computer; (iii) evidence existed of a possible *H. somnus* disease problem in previous years; (iv) management wanted to examine objectively the efficacy of the bacterin.

SUBJECTS

A total of 10,723 calves were followed during the winter of 1985-86; these auction market purchased calves were delivered to the feedlot in 167 separate groups. The mean number of calves per purchased group was 64.5 (range: 2-295). Each purchased group was kept intact throughout the trial. The calves were placed into 36 separate pens containing 300 calves (SD = 21.90; range 206-320) per pen. Individual pens required a mean 6.5 days (SD = 7.08) to fill; the mean number of purchased groups per pen was 4.7 (SD = 1.98). A pen, once full, was designated a "lot" and received no additions of new animals for the duration of the feeding period.

Of the 10,723 total, 7423 were steer calves and 3300 were heifer calves. The steers were purchased in 101 groups, averaging 73.5 calves per group; these steers were placed in 25 pens which were filled in a mean time of 4.9 days (SD = 2.48) containing an average 4.1 processing groups (SD = 1.45; range 1-7). The heifers were purchased in 67 groups averaging 50 calves per group; these heifers were placed in 11 pens which were filled in a mean time of 10.2 days (SD = 11.81) containing an average of 6.1 processing groups (SD = 2.39; range 3-10).

PROCESSING AND ALLOCATION OF TREATMENT

Initial processing was performed within 24 h of arrival at the feedlot. All calves were eartagged (color coded and numbered so that each calf was individually identified), branded, given 2 mL vitamin AD (Poten AD, rogar/STB, Pointe Claire-Dorval, Quebec) and 2-3 oz trichlorfon (Neguvon, Haver-Lockhart, Bayvet, Shawnee, Kansas). Heifers were implanted with a testosterone estradiol implant (Heifer-oid, Boehringer Ingelheim Animal Health, St. Joseph, Missouri); steers were implanted with a progesterone estradiol implant (Steer-oid, Boehringer Ingelheim Animal Health). Each purchased group was counted prior to processing and divided in two. Treatment was assigned arbitrarily to the first or second half of the group: this half became identified as the treatment or "*H. somnus* vaccinated" (HsV+) cohort; the remaining half was identified as the control or "*H. somnus* vaccine-negative" (HsV–) cohort.

Treatment (HsV+) calves were vaccinated with 2 mL of a combined infectious bovine rhinotracheitis (IBR)/parainfluenza (PI3) vaccine and *H. somnus* bacterin (IBR-PI3/Somnugen, Boehringer Ingelheim Animal Health) intramuscularly at processing. Control (HsV–) calves were vaccinated with 2 mL of an IBR/PI3 vaccine (Rhivax P, MTC Pharmaceuticals, Mississauga, Ontario) with no *H. somnus* bacterin. A mean 12.9 days (n = 36 pens; range 6-18 days; SD = 2.419) after the final purchased group was processed and introduced to a pen, all calves in the pen were revaccinated. This time HsV+ calves were vaccinated with 5 mL of a combined *H. somnus*/7-way *Clostridal* bacterin (Fermicon 7/Somnugen, Boehringer Ingelheim Animal Health) intramuscularly, and HsV– calves were vaccinated with 5 mL of a 7-way *Clostridial* bacterin (Clostri-Bac 7, Haver-Lockhart, Bayvet, Shawnee, Kansas) intramuscularly.

Each pen contained approximately 150 HsV+ calves and 150 HsV– calves. A total of 5357 calves were vaccinated with the *H. somnus* bacterin (HsV+ calves) and 5366 calves were not vaccinated (HsV– calves). There were 3712 and 1645 HsV+ steers and heifers respectively; there were 3711 and 1655 HsV– steers and heifers respectively.

A number of calves in certain pens were disqualified from the analysis because they did not fit into either cohort group. Forty-seven calves in pen 71 were removed from the study because they were ranch calves known to have been vaccinated prior to transport to the feedlot. Two purchased groups in pen 87 (numbering

32 and 53 calves) were disqualified because they were not properly divided at processing; one entire group received the bacterin, the other group did not. For the same reason, 77 calves were disqualified in pen 88. Three dead calves had lost their eartags and could not be identified for the purposes of analysis.

MORTALITY DATA

A complete necropsy was performed on all mortalities within 24 h of death. A gross diagnosis was recorded for each case and entered into the feedlot computer. When specific pathogens were suspected, or the diagnosis was tentative, appropriate tissue samples were harvested and sent to the Alberta Agriculture Veterinary Pathology Laboratory in Airdrie for histopathology and microbiology.

The necropsy diagnosis for each calf was placed into one of fourteen categories. This categorization depended upon the gross, histological, and microbiological diagnoses. These fourteen categories were then organized into two groups: the first group consisted of nine diagnostic categories in which involvement of *H. somnus* was considered biologically possible; the second group consisted of the remaining five diagnostic categories in which *H. somnus* involvement was considered extremely unlikely. This distinction allowed for a tighter case definition where a *H. somnus* bacterin would be expected to have an effect.

MORTALITY ANALYSIS

All gross necropsy, histopathology, microbiology, vaccine status, and case history data were collected and entered into a data-base manager program (Reflex, the Analytic Database System, Borland/Analytica Inc.). Preliminary analyses by cross-tabs were performed, followed by stratified and contigency table analyses (13,14). Feedlot processing sheets, feedlot computer case summaries, gross necropsy records, and laboratory reports were cross-referenced to check for data accuracy.

Bacterin effects were analyzed in several ways. First, mortality was stratified by time so the number of deaths occurring in each cohort per unit time could be examined. The day on which a calf died was corrected for arrival date so that all mortality dates indicated the number of days between arrival at the feedlot and death. Total crude mortality, total disease-specific mortality, and total time-specific mortality were then calculated for both cohorts: statistical contingency table analysis followed.

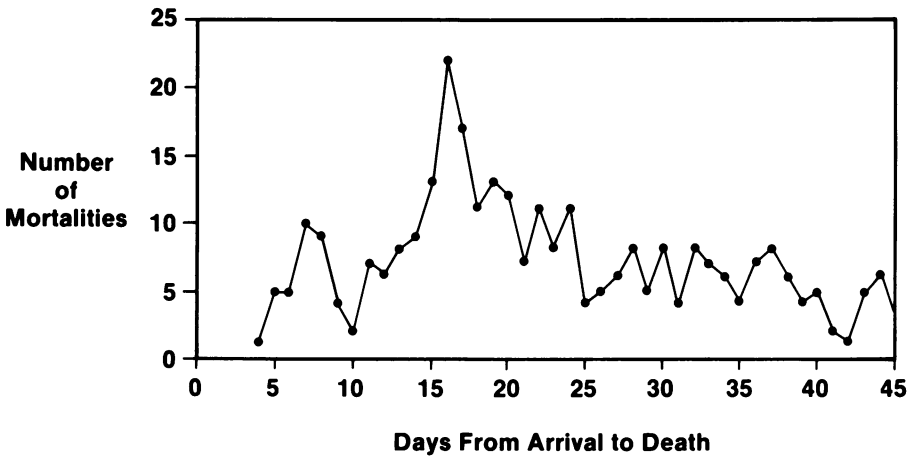


Fig. 1. Mortality curve for day 0 to day 45.

Second, time-specific incidence rates of fatal disease (IFD) were examined. The day of first treatment of all calves that subsequently died was recorded as the day of fatal disease onset (FDO). The IFD for each time period was calculated for each cohort, and the incidence rate ratio of fatal disease (IRFD) for HsV- versus HsV+ calves was determined using the appropriate denominator of bovine time and a radix of 10,000. Confidence intervals about the IRFD were calculated using the test-based method which is known to perform well for rate ratio limits when the rate ratio is between 0.2 and 5.0 (13).

Finally, examination of the effects of calf sex, specific necropsy diagnosis, and purchased group size on cohort mortality and the IRFD was performed. Calculation of the attributable risk percent was as described by Martin *et al* (15).

MASS MEDICATION

Feedlot management policy was to treat all the calves in a pen with an antibiotic once the cumulative bovine respiratory disease (BRD) morbidity reached 10% for that pen. The winter

TABLE I. Distribution of the Different Classes of Necropsy Diagnosis for the Entire Feeding Period

Necropsy Diagnosis	Number of Cases	Percent of Total Mortality	Hemophilosis Possible[a]
1. Fibrinous pneumonia	226	49.2	+
2. Intersitial pneumonia	37	8.1	-
3. Bloat	36	7.8	-
4. Enteric	33	7.2	-
5. Other (fractures etc.)	23	5.0	-
6. Mixed pneumonia	20	4.4	+
7. Bronchopneumonia	18	3.9	+
8. Cardiac (fib pericar etc.)	17	3.7	+
9. Nervous (no TEME confirmed)	15	3.3	+
10. Polyarthritis	11	2.4	+
11. Pleuritis	11	2.4	+
12. TEME confirmed	8	1.7	+
13. Lung abscessation	2	0.4	+
14. Upper respiratory	2	0.4	-

[a]"+" means the diagnosis could have had *Haemophilus somnus* associated with it. "-" means the diagnosis was very unlikely to have had *Haemophilus somnus* associated with it

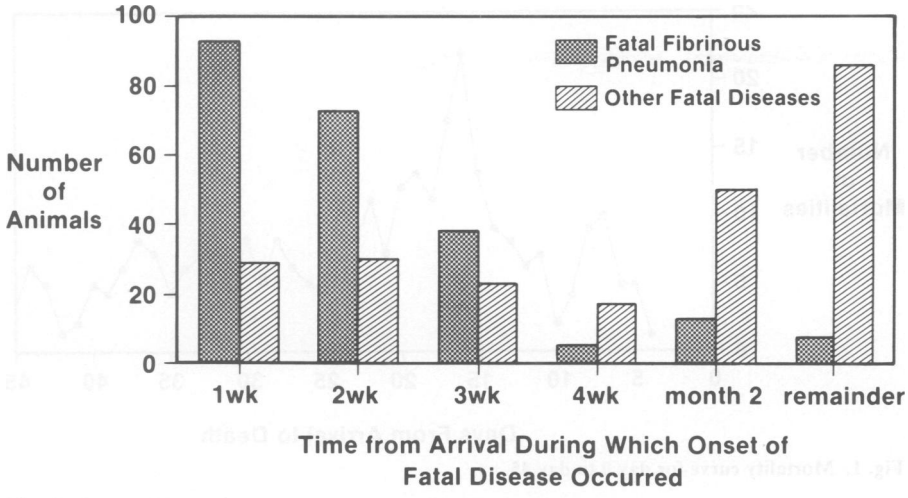


Fig. 2. Onset of fatal disease by time period and disease.

of the trial was particularly severe with respect to BRD: 32 of 36 pens in the study were mass medicated. Ten percent morbidity was reached rapidly in most of the pens. As a result, calves in a pen were mass medicated a mean 5.3 days after the last purchased group entered the pen (range: -2 to 14 days, -2 because some pens were mass medicated before they were filled). The following antibiotics were used: a combination long and short acting injectable oxytetracycline in 17 pens; a combination long and short acting injectable penicillin in eight pens; injectable long acting penicillin in four pens; sulfas in water or feed in three pens. Four pens were left unmedicated.

RESULTS

GENERAL

A total of 459 calves (4.3%) died during the 37 wk feeding period. Peak mortality occurred on day 16, decreasing rapidly thereafter (Fig. 1). Overall, fibrinous pneumonia was the most common necropsy diagnosis (Table I). Fibrinous pneumonia was the predominant necropsy diagnosis for mortalities that first became sick during the initial three weeks in the feedlot (Fig. 2). This diagnosis accounted for 80% of the mortality in the first month, 35% in the second month, decreasing to less than 20% per month after the fourth month.

Fatal disease onset (FDO) peaked on day 4 (Fig. 3), with a geometric mean (which adjusts for the skewed nature of the data) of 16 days. Twenty-six percent of the calves that died became sick initially within the first seven days of arrival at the feedlot; a further 22% became fatally ill during the second week. Therefore, by the time mortality reached its highest point on day 16, fully 48% of the calves that were going to die were already ill.

COHORT DIFFERENCES

Over the entire feeding period, 247 HsV- calves (4.60%) and 212 HsV+ calves (3.95%) died. This represents a total crude mortality difference of 35 calves, or 0.65% (95% confidence interval (CI): -0.12, 1.4). The total crude mortality difference for steers was 28 calves (0.76%; 95% CI: -0.13, 1.6) and for heifers was six calves (0.30%; 95% CI: -1.1, 1.8). None of these total crude mortality differences was significant.

Total crude and time-specific crude mortalities are presented (Table II). Confidence intervals not including unity indicate a significantly ($p < 0.05$) greater mortality in the HsV- calves: this occurred during the second week, the second month, and during the first two months inclusive.

The IRFD in HsV- versus HsV+ calves was 1.61 ($p < 0.05$) during the second week, and 1.95 ($p < 0.05$) during the second month (Table III); during this time 36% of FDO occurred. The IFRD for other periods did not differ significantly from one. The IFD averaged over day 7 to 56, during which over 50% of the FDO occurred, was 1.34 times higher ($p < 0.05$) in the HsV- calves.

SEX AND NECROPSY DIAGNOSIS AS MODIFIERS

The epidemiology of fatal disease and cohort bacterin effects differed for heifer calves compared to steer calves. Heifer calves demonstrated a significantly ($p < 0.01$) greater IFD during the first week, a trend which continued for the second through the fourth week (Table IV, Fig. 4). Therefore, during the period of greatest IFD for the feeding period, heifer calves were at greater risk of developing fatal disease. The resulting overall mortality of heifer calves (164/3300 = 4/97%) was one full percent higher than that for steer calves (294/7423 = 3.96%).

The bacterin tended to reduce FDO for steers during the first two months; an IRFD significantly greater than

TABLE II. Time Specific Crude Mortality

Time Period	Mortality (No.) HsV-[a]	Mortality (No.) HsV+[a]	MRR[b]	95% C.I.[c]
1st week	4	7	0.57	(0.17-1.91)
2nd week	33	13	2.53[e]	(1.37-4.67)
3rd week	51	46	1.11	(0.75-1.65)
4th week	21	31	0.68	(0.39-1.18)
2nd month	71	44	1.61[d]	(1.17-2.32)
Arrival-9 week	180	141	1.27[d]	(1.03-1.57)
9th week-end	67	67	1.01	(0.72-1.41)
Arrival-end	247	212	1.16	(0.97-1.38)

[a]HsV- = unvaccinated calves; HsV+ = vaccinated calves
[b]MRR = mortality rate ratio of HsV- verus HsV+ calves
[c]95% C.I. = 95% confidence interval
[d]$p < 0.05$
[e]$p < 0.01$

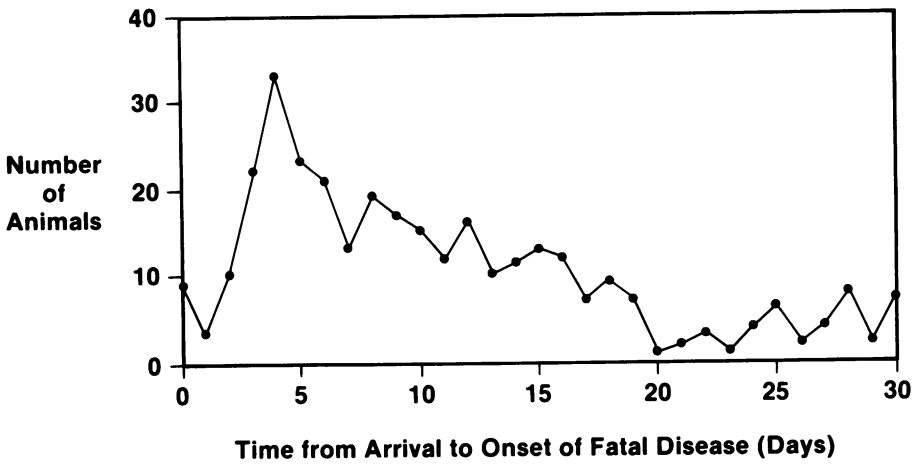


Fig. 3. Morbidity curve for fatal cases (time from arrival to onset of fatal disease).

one ($p < 0.05$) occurred during the second week (Table V), a period during which the IFD was at its second highest. In contrast, the bacterin did not significantly reduce FDO for heifer calves during the first month after arrival at the feedlot (Figs. 5 and 6). The bacterin did reduce FDO for heifers during the second month, during which 14% of FDO began. Once mortalities probably not associated with *H. somnus* (for example, a fractured femoral neck) were removed from the analysis, steer HsV- mortality rate (MR) was significantly ($p < 0.05$) greater than steer HsV+ MR (Table VI); however this difference was not evident in the heifer calves. The attributable percent overall for steer calves was 17.4%; this suggests that 17.4% of fatal respiratory disease in unvaccinated steers could have been prevented by vaccination with the *H. somnus* bacterin upon arrival at the feedlot.

The presence of *H. somnus* was confirmed by histopathology or microbiology in 25 out of 448 (5.6%) cases. Of these cases, 17 were HsV- calves and eight were HsV+ calves ($RR = 2.1$, $p > 0.05$), indicating a trend, but not a significant difference.

The size of the original purchased group was found not to be a modifier of bacterin effect.

DISCUSSION

Epidemiological analysis of vaccine efficacy in the calf feedlot presents several problems. Epidemic curves of calf morbidity in North American feedlots demonstrate that the greatest proportion of morbidity often occurs within two to three weeks of arrival at the feedlot (16,17). In this trial, one-quarter of the total fatal disease onset (FDO) occurred during the first week. A large proportion of calves, therefore, became ill before a vaccine given upon arrival could have taken effect. This early high morbidity of feedlot calves emphasizes the importance of choosing an appropriate effect measure for vaccine efficacy and paying particular attention to the morbidity and mortality of individuals and groups during the first two weeks. Several epidemiological effect measures exist for determining vaccine efficacy including crude morbidity, crude and cause-specific mortality, and incidence rates of fatal disease (IFD). Advantages and disadvantages exist for each.

Crude morbidity can be recorded and differences between vaccinated and unvaccinated cohorts determined. Given the speed with which sick calves must be treated in large feedlots, and our present diagnostic technology, this measure is truly crude; no accurate method of determining cause-specific morbidity exists. Mortality may be a better measure of vaccine effect, if one includes enough calves in the study, and the disease or complex of diseases against which the vaccine is used is a component of a significant sufficient cause or causes of mortality (5). Mortality is easy to diagnose without controversy and a specific cause of mortality can be determined with far greater accuracy than for morbidity. However, three distinct problems exist. First, necropsy findings give a prevalence of end-causes of death as opposed to causes of the onset of fatal disease. Without the initiator of the disease, the end-cause may not have had a chance to kill the animal. Second, when calves are not vaccinated until arrival their time of death could be misleading; calves that die on day 14 after arrival may have become fatally sick on day 5, before the vaccine had a chance to become protective. Finally, mortality may underestimate the impact of diseases having a low case fatality risk because this measure represents only the most extreme effect of the disease (7).

We have introduced incidence rate of fatal disease (IFD) as an epidemiological effect measure to be used in addition to mortality rate (MR). Such a measure is only made possible by the careful individual identification and event recording for each calf. The IFD

TABLE III. Incidence Rates (IFD) and Incidence Rate Ratios (IRFD) for Fatal Disease for the Entire Feedlot

Time Period	IFD[a]	IRFD[b]	95% C.I.	Proportion of Resulting Mortality
1st week	112.84	1.05	(0.73-1.52)	0.26
2nd week	95.22	1.61[c]	(1.09-2.38)	0.22
3rd week	56.55	0.89	(0.57-1.39)	0.13
4th week	20.85	0.69	(0.29-1.62)	0.05
2nd month	14.72	1.95[c]	(1.17-3.26)	0.14
3rd month-end	3.03	0.92	(0.61-1.38)	0.20
2nd-8th week	33.15	1.34[c]	(1.04-1.72)	0.54

[a]IFD = incidence rate (number of new cases of fatal disease per 10,000 bovine feedlot weeks)
[b]IFRD = incidence rate ratio of fatal disease in HsV- versus HsV+ calves
[c]$p < 0.05$

TABLE IV. Incidence Rate Ratio for Fatal Disease Comparing Sexes. Incidence Rates for Steers and Heifers Are Also Listed

Time Period	Steers IFD[a]	Heifers IFD[a]	IRFD[b]	95% C.I.
1st week	91.61	160.61	1.75[c]	(1.23-2.49)
2nd week	87.66	109.19	1.25	(0.83-1.89)
3rd week	44.90	82.80	1.84	(0.23-14.99)
4th week	19.13	24.74	1.29	(0.55-3.05)
2nd month	15.40	13.17	0.86	(0.50-1.47)
3rd month-end	3.05	2.58	0.75	(0.47-1.21)
2nd-8th week	30.49	38.72	1.27	(0.98-1.64)

[a]IFD = incidence rate (number of new cases of fatal disease per 10,000 bovine feedlot weeks)
[b]IRFD = incidence rate ratio of fatal disease in heifer calves versus steer calves
[c]$p < 0.01$

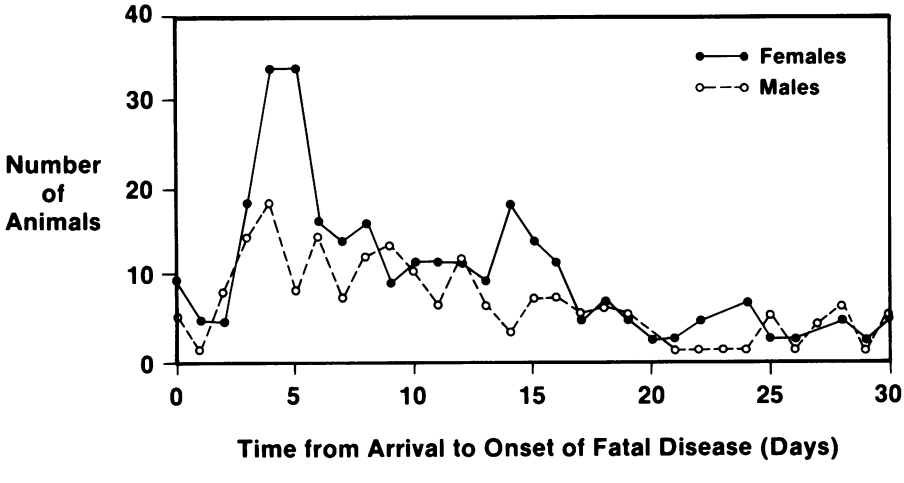
gives a much clearer picture of when initiating factors in fatal disease are occurring and allows the investigator to identify calves which became fatally sick before the vaccine could take effect; this addresses the first two problems identified for the use of the mortality rate, but not the third. Like the MR the IFD will probably underestimate the effect of a vaccine that is, in fact, efficacious.

Comparison between vaccinated and unvaccinated cohorts with either effect measure used in this study (MR or IFD) supports the hypothesis that a beneficial effect results from the use of a *H. somnus* bacterin in steer calves immediately upon arrival at the feedlot. Time after arrival and sex of the calf were modifiers of the bacterin effect; the beneficial response was predominant during the second week after arrival in steer calves while no protection was clearly evident in heifer calves.

Certain characteristics of this study design may have biased the results towards a finding of no bacterin effect. First, the calves were not vaccinated until arrival in the feedlot after many of the sufficient causes of pneumonic pasteurellosis had ample opportunity to take effect. This was not a limitation of the study per se, but a limitation set by the established structure of the North American beef feeding system. Second, mixing HsV+ and HsV- calves in the same pen could have resulted in one of two scenarios: (i) immunity developed in the HsV+ cohort acted to protect the HsV- cohort by reducing the susceptible proportion of in-contact animals and reducing their pen density (18); (ii) disease in the HsV- calves overwhelmed the protective effect of the bacterin in the HsV+ calves. Either scenario would result in a decreased difference in mortality between cohorts, reducing the perceived effectiveness of the bacterin. A third element which may have worked against demonstrating a reduced mortality rate in the HsV+ cohort was the mass medication of all calves in 32 of 36 pens. This procedure could have reduced the mortality of susceptible HsV- calves if they were just becoming affected by a *H. somnus* disease which was responsive to an antibiotic when they were mass medicated.

Conversely, three factors could have acted to increase the mortality rate difference between the cohorts. First, all calves were given an IBR-PI3 vaccine on arrival. If the IBR-PI3 vaccine increased the risk of BRD morbidity and mortality as suggested by the Bruce County study (7-9), then the effectiveness of the bacterin may have been exaggerated compared to a feedlot in which respiratory vaccines such as IBR-PI3 are not used immediately upon arrival. Second, overall mortality was particularly high during the study compared to previous trials which had crude mortality rates of less than two percent (7-12); in a year with lower overall mortality the absolute cohort difference would probably be smaller. Third, pushing all the calves through the chute a second time two weeks after arrival could have increased the risk of mortality in the HsV- cohort. In fact, the opposite of the latter occurred; during the third and fourth weeks the HsV+ calves had a higher IFD than HsV- calves.

Awareness of three further design characteristics are important for considering the validity of this study. First, this was not a controlled field trial in which the vaccine was assigned by a formal random procedure to the feedlot calves. Instead, all calves which had arbitrarily been vaccinated with the *H. somnus* bacterin by the feedlot health management crew were identified and followed, as were all animals arbitrarily not vaccinated with the bacterin. Prospective follow-up studies such as this one are more likely to contain some element of bias



Note: Heifer population adjusted to 7423 to coincide with steer population.

Fig. 4. Morbidity curve for fatal cases by sex.

TABLE V. Incidence Rate Ratio (IR) for Fatal Disease Onset (FDO) Categorized by Sex

Time Period	Steers IRFD[a]	95% C.I.	Heifers IRFD[a]	95% C.I.
1st week	1.13	(0.69-1.84)	0.96	(0.58-1.58)
2nd week	1.71[b]	(1.04-2.82)	1.39	(0.72-2.67)
3rd week	1.20	(0.61-2.36)	0.59	(0.28-1.26)
4th week	1.00	(0.33-3.09)	0.33	(0.07-1.52)
2nd month	1.51	(0.83-2.73)	4.63[b]	(1.49-14.39)
3rd month-end	0.87	(0.54-1.40)	1.09	(0.47-2.54)
2nd-8th week	1.46[b]	(1.07-2.00)	1.14	(0.75-1.72)

[a]IRFD = incidence rate ratio of fatal disease in HsV- versus HsV+ calves
[b]$p < 0.05$

than randomized field trials; bias could reduce the similarity of the cohorts, and distort vaccine effects. However, the arbitrary procedure itself, where one-half of each processing group received the vaccine, and the large number of sources of auction market calves that made up each processing group, made unlikely the possibility of a significant bias occurring. Second, the entire feeding period was broken down into a number of smaller periods based upon the pattern of fatal disease onset demonstrated in Fig. 2. This greatly enhanced the examination of the bacterin effect during the periods of greatest risk, and helped to separate the impact of the first week. This enhancement is tempered by the increased possibility of committing a type I error, in the week by week analysis, where a vaccine effect deemed significant may actually have occurred by chance alone (19). Third, the two cohorts received IBR vaccines produced by two different companies. Because there was no evidence to the contrary, the assumption was made that the two IBR vaccines were biologically identical and MR or IFD differences between cohorts were entirely a result of the presence or absence of *H. somnus* in the vaccine. If this assumption was not correct the differences between cohorts could have been a result of IBR vaccine differences.

The finding that fibrinous pneumonia was the most common postmortem diagnosis is in agreement with the results of other feedlot calf (7-9) and yearling (20-22) postmortem studies. However, little has been published about a difference between steer and heifer calves in fatal disease pattern or response to *H. somnus* vaccination. In this study, calf sex was a modifier of bacterin effect: vaccination of heifer calves, unlike steer calves, did not reduce their mortality risk. Several possible reasons exist for this apparent difference. There were fewer than half the number of heifer calves than steer calves in this trial: consequently, confidence intervals for effect measures in heifers were much wider and the point estimates less precise. With this warning in mind, it is still helpful to consider the differences. It is unlikely, even in calves that develop a rapid anamnestic response, that the bacterin would have a noticeable protective effect were FDO occurs during the first week. A significantly greater proportion of heifer IFD occurred during this time; it therefore seems likely that in this trial a larger proportion of heifers were simply not at risk to diseases preventable by giving a *H. somnus* vaccine upon arrival at the feedlot. How common such a sex difference in IFD is at feedlots is unknown and deserves further study. Other differences between sexes which may have altered the fatal disease pattern or affected the bacterin efficacy include the following: heifer calves arrived in smaller groups and their pens took longer to fill; heifers have different endogenous hormones and received a different implant upon arrival.

The protective effect during the second week occurred before the second vaccination. Several explanations exist for this finding. First, one vaccination may have provided sufficient immunity rapidly enough in immuno-naive calves to be protective. Alternatively, one vaccination may not have protected immuno-naive calves during the second week, but the number of calves previously exposed to the *H. somnus* bacterium or bacterin which had a subsequent rapid anamnestic response may have been sufficient to be protective. Finally, both a rapid immunity in immuno-naive calves and an anamnestic response in previously exposed calves may have occurred. Which of these possible explanations was most likely is difficult to determine without a concomitant serological study where

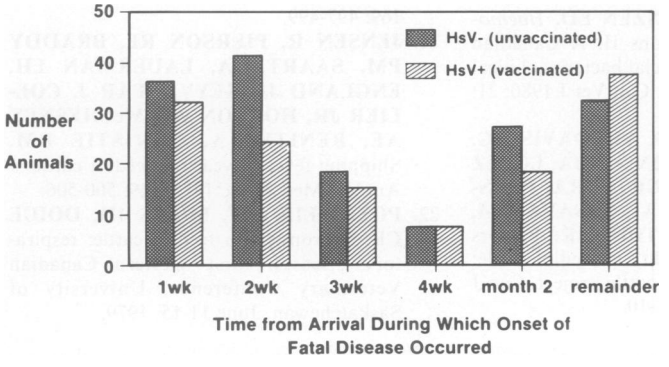


Fig. 5. Onset of fatal disease for steers by time period and vaccine status.

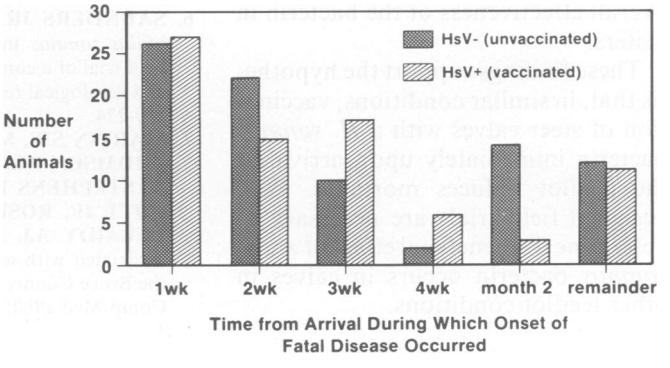


Fig. 6. Onset of fatal disease for heifers by time period and vaccine status.

TABLE VI. Mortality Rate Ratios Comparing Sexes for Selected Diagnostic Categories

Necropsy Diagnosis	MRR[a] (95% confidence interval)	
	Steers	Heifers
Fibrinous pneumonia	1.27 (0.89-1.82)	1.01 (0.76-1.33)
H. somnus:		
Possible	1.36 (1.03-1.79)[b]	1.04 (0.75-1.45)
Unlikely	0.96 (0.64-1.43)	1.19 (0.60-2.35)
All diagnoses	1.21 (0.97-1.51)	1.07 (0.79-1.36)

[a]MRR = mortality rate ratio for HsV- (unvaccinated) versus HsV+ (vaccinated) calves
[b]Significant ($p < 0.05$)

high serum titers are assumed to be correlated with protection; such a study was not possible during the trial.

Given our finding of a protective effect during the second week in the feedlot, at least in steers, it is possible that inclusion of a *H. somnus* bacterin in a cow-calf preimmunization program would reduce the proportion of the IFD which occurs during the first week in the feedlot. Since the first week is frequently the most significant time for FDO, use of an efficacious *H. somnus* bacterin before arrival could be an important method of reducing first week IFD. Well conducted field trials are necessary to test this hypothesis.

In conclusion, crude mortality and IFD during the second week in the feedlot were reduced significantly in the steer HsV+ cohort. Over the entire feeding period, once mortalities which were probably not associated with hemophilosis were removed from the analysis, steer HsV+ calves had a significantly lower MR. The findings suggest that approximately 17% of the mortality in unvaccinated steers could have been prevented by vaccination. The bacterin had a protective effect in heifers during the second month, but a higher IFD during the first week than in steers may have acted to reduce the overall effectiveness of the bacterin in heifers.

These findings support the hypothesis that, in similar conditions, vaccination of steer calves with a *H. somnus* bacterin immediately upon arrival at the feedlot reduces mortality. Well designed field trials are necessary to determine if a beneficial effect of an *H. somnus* bacterin occurs in calves in other feedlot conditions.

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