ARTICLES

An evaluation of antimicrobial therapy for undifferentiated bovine respiratory disease

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Abstract

A field trial of antimicrobial therapy for cases of undifferentiated bovine respiratory disease (UBRD) in beef calves was conducted at four Ontario feedlots. The primary purpose of the trial was to evaluate the efficacy of three different antimicrobials (oxytetracycline, penicillin, and trimethoprim-sulfadoxine) in the treatment of UBRD occurring within the first 28 days postarrival.

The response, relapse, and case fatality rates overall were 85.7%, 14.8%, and 1.4%, respectively, and were not significantly different among the three antimicrobials evaluated. Weight gains of calves treated with the different drugs were not statistically different over the feeding period. Calves that suffered a relapse posttreatment were first treated significantly earlier ($p < 0.001$) in the postarrival period than those that did not relapse. Considered together, treated calves gained significantly less ($p < 0.05$) over the first 28 days and throughout the entire feeding period than controls that were never sick. Cases of UBRD that responded to therapy and did not relapse had rates of gain that were not significantly different from the controls.

Résumé

Évaluation d'un traitement antimicrobien pour la maladie respiratoire non différenciée

Une étude sur le terrain fut effectuée dans quatre parcs d'engraissement en Ontario afin d'établir l'efficacité d'un traitement antibactérien pour les cas de maladie respiratoire bovine non différenciée chez les veaux. Le but de cette expérimentation était d'évaluer l'efficacité de trois agents antimicrobiens (oxytétracycline, pénicilline et triméthoprime-sulfadiazine) pour le traitement de maladie respiratoire bovine non différenciée survenant durant les 28 premiers jours après l'arrivée.

La réponse au traitement, le taux de rechute et le taux de mortalité furent respectivement de 85,7 %, 14,8 %, 1,4 % et il n'y a pas une différence significative entre les trois agents évalués. Le gain de poids chez les veaux traités ne fut pas statistiquement différent entre les groupes durant la période d'engraissement.

Les veaux qui ont fait une rechute après traitement furent traités de façon significative ($p < 0,001$) plus tôt après leur arrivée comparativement à ceux qui n'ont pas fait de rechute. Dans l'ensemble, les veaux traités ont eu un gain de poids plus bas de façon significative ($p < 0,05$) durant les 28 premiers jours et pour toute la durée de l'engraissement si on les compare au groupe témoin qui n'a jamais démontré de signes de maladie. Les cas de maladie respiratoire ayant répondu au traitement et n'ayant pas subi de rechute ont démontré un gain de poids de façon non significative comparativement aux sujets du groupe témoin.

(Traduit par Dr Thérèse Lanthier)

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Introduction

Respiratory disease, especially bacterial pneumonia, is the single most important cause of morbidity and mortality among feedlot cattle in North America (1-4). The importance of respiratory disease as a cause of losses to the feedlot industry of North America has been discussed at great length and documented many times. Although direct losses such as mortality are readily calculated, indirect costs such as drugs, labor, veterinary services, and performance effects are more difficult to substantiate. Without evidence of these costs and *in vivo* evaluation of alternative preventive and therapeutic strategies, logical health management programs for the control of bovine respiratory disease cannot be proposed.

Despite the fact that numerous antimicrobials have been advocated as useful for therapeutic purposes, few have been evaluated in an appropriate manner in field trials (5). Other attempts at assessing efficacy have utilized small numbers of animals (6), an unrealistically low dosage of one of the antimicrobials (7), or had no comparison group (8).

The primary objective of this study was to determine if there were differences in the response rates and other measures of efficacy when three commonly used antimicrobials were utilized for therapy of undifferentiated bovine respiratory disease (UBRD) in feedlot calves in southern Ontario. Secondary objectives were

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Table 1. Rates of UBRD and mortality in four Ontario feedlots

Location	No. of calves received	Treatment rate[a] (%)	Mortality rate (%)	Case fatality rate (%)
1 Private	360	148/360 (41.1)	1/360 (0.3)	1/148 (0.7)
2 Private	204	54/204 (26.5)	0/204 (0.0)	0/54 (0.0)
3 EBRC 1984	228	54/228 (23.7)	2[b]/228 (0.9)	1/54 (1.8)
4 RCAT 1984	155	30/155 (19.3)	0/155 (0.0)	0/30 (0.0)
5 EBRC 1985	97	50/97 (51.5)	2/97 (2.1)	2/50 (4.0)
6 RCAT 1985	135	72/135 (53.3)	1/135 (0.7)	1/72 (1.4)
Total	1179	408/1179 (34.6)	6/1179 (0.5)	5/408 (1.2)

[a]Percentage of calves treated (first treatments only)
[b]One calf died before being treated

to describe the effects of treatment on performance (weight gain) and, within the treated calves, the characteristics and performance of animals that did not respond or which relapsed.

Materials and methods

Study farms and animals

Eleven hundred and seventy-nine beef calves were observed for a period of 28 days following their arrival in four different southern Ontario feedlots during the late autumn of 1984 and 1985. The calves were born during the months of March, April, and May on farms and ranches in Manitoba, Saskatchewan, Alberta, and British Columbia. Following weaning, the animals were either transported directly from the farm of origin to Ontario or, as in the majority of cases, passed through auction markets prior to transport. Calves travelled by train and truck, or entirely by truck, arriving in the Ontario feedlots in October and November. Approximately 450 of the calves were heifers, with the remainder being almost exclusively steer calves. There were approximately 20 bull calves in total. None of the calves originated from sales or farms that advertised or identified (via eartag) these animals as part of any preconditioning or prevaccination program. Four feedlots participated in the study in 1984 and, of these, the two academic research facilities were involved again in 1985. Approximately 100 of the 615 calves in the two research station feedlots had horns. These were removed at or after the end of the 28 day postarrival observation period. In addition, as many as 20% of calves at the other two feedlots had horns which the owners elected not to remove.

Two private commercial feedlots accounted for 564 of the calves under observation in 1984. At location 1, 360 calves were under observation and arrived in six different groups over the period October 27, 1984 to November 9, 1984. The groups varied in size from 18 to 94 calves. All calves were housed together postarrival on a concrete yard with renovated bank barns for shelter. Facilities were not available to record weights of these calves. No handling or processing was imposed during the 28-day trial period other than for treatment of respiratory disease. At first treatment, each sick calf received a numbered eartag, and an individual health record was initiated. Sick calves were confined to a separate pen until their course of treatment was completed. At location 2, again a private feedlot, housing conditions were similar to location 1. Two hundred and four calves were included in the study here. These calves arrived in three groups of 54, 49 and 101 on November 1, 2 and 10, 1984. Again, no handling other than for treatment of UBRD occurred until after the 28-day period was complete. Calves at both of the above locations were allowed free access to dry hay for the first two weeks, after which corn silage was gradually introduced to their diet over the next two weeks.

At the two research station feedlots, Elora Beef Research Centre (EBRC) and Ridgetown College of Agricultural Technology (RCAT), calves were weighed, eartagged, and assigned by formal randomization to pens within one to five days postarrival with the average elapsed time being two days.

Four groups (228 calves) were under observation at EBRC in 1984 and two groups (97 calves) in 1985. These calves were housed on slatted floors with four animals per pen from arrival until completion of the feeding period, which varied from 138 to 183 days. (The cattle were allocated to different nutrition studies after the initial 28 day trial period.) The cattle received dry hay *ad libitum* for one day after which a mixture of haylage and corn silage was introduced. By ten days postarrival, calves were no longer receiving any dry

Table 2. Response, relapse, and case fatality rates for UBRD at feedlots in Ontario in a clinical trial of three antimicrobials

Location	No. of treated calves included on trial	Response[a] rate (%)	Relapse[b] rate (%)	Case fatality rate (%)
1 Private	118	98/118 (83.0)	10/98 (10.2)	1/118 (0.8)
2 Private	42	38/42 (90.5)	11/38 (28.9)	0/42 (0.0)
3 EBRC 1984	51	40/51 (78.4)	2/40 (5.0)	1/51 (2.0)
4 RCAT 1984	30	27/30 (90.0)	7/27 (25.9)	0/30 (0.0)
5 EBRC 1985	50	42/50 (84.0)	7/42 (16.7)	2/50 (4.0)
6 RCAT 1985	72	66/72 (91.7)	9/66 (13.6)	1/72 (1.4)
Total	363	311/363 (85.7)	46/311 (14.8)	5/363 (1.4)

[a]Percentage with temperature < 40°C by day 3 of treatment
[b]Of those that responded to first course of therapy

hay and were allowed full feed of the silage/haylage combination plus appropriate protein, vitamin, and mineral supplementation until the end of the 28-day period. At that time, pens of calves were assigned on a formal random basis to different test rations. A third weight was taken before slaughter or sale for the purposes of this trial.

All processing at EBRC both in 1984 and 1985 occurred at the time of the second weighing, approximately 28 days postarrival. Procedures performed at this time, in addition to weighing, included dehorning as required, Synovex-S (Syntex Agribusiness, Mississauga, Ontario) implanting, injection of ivermectin (Ivomec, MSD Agvet, Kirkland, Quebec) as an anthelmintic/grubicide treatment, and vaccination with an intramuscular modified live IBR/PI3 vaccine (Resbo IBR/PI3, Norden Laboratories, Lincoln, Nebraska).

At RCAT, three groups of cattle (155 calves) were under study in 1984 and one group (135 calves) in 1985. Calves were allowed free access to hay for a week and then during the next seven days were gradually started on a silage and/or haylage ration appropriately supplemented with cracked corn, protein, and vitamin/mineral premixes. The calves were housed seven or eight animals per pen in a totally sheltered but not enclosed barn. At the end of the 28-day introduction and observation period, calves were weighed individually and each pen was randomized to one of several test rations. In 1984, final weights were taken at slaughter which occurred 193 to 235 days after the first weighing depending upon the finishing characteristics of the calves. In 1985, the third weight was taken 145 days following the initial one. In 1984, all calves at RCAT were processed at the time the first postarrival weight was taken. Processing included weighing, eartagging, implanting with estradiol (Compudose, Elanco, London, Ontario), and deworming with ivermectin. Dehorning for those calves requiring this procedure occurred two weeks later. In 1985, eartagging and weighing occurred two days postarrival. Processing, which consisted of implanting with Synovex-S (Syntex), deworming with levamisole (Tramisol, Cyanamid, Toronto, Ontario), application of the grubicide fenthion (Spotton, Bayvet, Rexdale, Ontario), and dehorning as required, was delayed until the time of the second weighing one month postarrival.

Case definition and treatment protocol

A standard protocol for detection of sick cattle was available at each location. The investigators stressed in the protocol that early detection was a crucial factor in the success of treatment, and the guidelines emphasized clinical signs that are believed to be exhibited early in the course of UBRD. The treatment protocol was identical across all locations. Calves suspected of being ill, based on signs such as depressed attitude, lack of rumen fill, and/or partial anorexia, were removed from the group and their rectal temperature obtained. If the temperature was ≥ 39.5°C, the calf was assigned, within a location, on a systematic random basis to receive as therapy one of three antimicrobials. Calves with temperatures < 39.5°C were not treated at this time. The products utilized on day 1 were oxytetracycline (Liquamycin LP, rogar/STB, London, Ontario) intramuscularly, with no more than 20 mL per site, at a dosage of 10 mg/kg of body weight (BW); procaine penicillin G (Ethacillin, rogar/STB, London, Ontario) subcutaneously in one site at 45,000 IU/kg BW; or trimethoprim-sulfadoxine (Trivetrin, Coopers Agropharm, Ajax, Ontario) at 3 mL/45 kg BW intramuscularly in one site. The

Table 3. Outcome of treatment with three antimicrobials used as first-line therapy for calves with UBRD

First therapy	Response rate at day 3 (%)	Relapse rate[a] (%)	Case fatality rate (%)
Oxytetracycline	106/123 (86.2)	14/106 (13.2)	1/123 (0.8)
Penicillin	100/114 (87.8)	14/100 (14.0)	1/114 (0.9)
Trimethoprim-Sulfadoxine	105/126 (83.3)	18/105 (17.1)	3/126 (2.4)
Total	311/363 (85.7)	46/311 (14.8)	5/363 (1.4)

[a]Of those that responded satisfactorily by day 3 to first course of therapy
No significant differences ($p > 0.10$)

trimethoprim-sulfadoxine product contained 40 mg trimethoprim and 200 mg sulfadoxine per mL. All drugs were administered at the above dosages once daily. At the two private feedlots, calves were confined to a hospital pen until finished a course of therapy, whereas at the two research facilities sick calves were housed in their home pens. On day 2, the assigned antimicrobial was repeated with no assessment of body temperature change. On day 3, 48 hours after therapy had commenced, the calf's temperature was recorded. A responder was defined as an animal that had a temperature at this time of $< 40°C$. If this was the situation, the antimicrobial was repeated that day and again on day 4. A case was deemed to be nonresponsive if the rectal temperature on day 3 was $\geq 40°C$. In 1984, therapy for nonresponders was changed to a four day course of chloramphenicol (Austicol, PVU, Victoriaville, Quebec) administered intramuscularly at 20 mg/kg BW every 12 hours. In 1985, because of a ban imposed by Health and Welfare Canada on the use of chloramphenicol in food-producing animals, therapy for nonresponders was changed on a systematic random basis to one of the other two antimicrobials being evaluated, and that drug administered for four days. Thus, for example, equal numbers of the trimethoprim-sulfadoxine treated, nonresponsive cases were allocated to oxytetracycline and penicillin for four days. Therapy with the second-line antimicrobial was for four days regardless of temperature response.

A relapse was defined as a case that, after being treated for either four days with the first-line drug or two days with the first-line drug and then an additional four days with a backup drug before treatment ceased, experienced a second occurrence of UBRD requiring antimicrobial therapy. This could occur one or more days after the initial round of therapy ceased. The same case definition was used as for the first treatment regime, that is, the calf had to have a fever $\geq 39.5°C$ as well as exhibit other signs of illness such as depression or anorexia. Animals relapsing less than ten days after commencing first treatment were treated with chloramphenicol (1984) or the appropriate randomly designated backup drug for that case (1985). If the relapse occurred $\geq$ 10 days after first treatment, the calf was retreated with the originally assigned antimicrobial. Since the nature of the products evaluated precluded the trial being conducted in a blind or double-blind manner, possible bias was avoided by an objective outcome measure (temperature). Compliance with the treatment protocol was enhanced by a minimum of semi-weekly visits by the investigator to the cooperating feedlots.

Calves at all feedlots were followed for a period of 28 days after arrival to record treatment-related data and the entire feeding period for respiratory-related mortality and, where available, weight gain performance.

All dead animals were necropsied at either the Ontario Veterinary College or at Veterinary Laboratory Services, Ontario Ministry of Agriculture and Food, Ridgetown, with the diagnosis based on gross and histological lesions as well as bacteriology of each case. When deemed relevant, samples were submitted for appropriate virological testing.

Sampling procedures

At EBRC and RCAT, 28 days postarrival, each calf treated for UBRD and an equal number of randomly selected control calves were weighed. Nontreated controls were selected utilizing a computer-based random number generator using A Programming Language (APL).

In 1984, when the proportion of treated calves at both EBRC and RCAT was less than 50% of the population, one-half of the controls came from pens where treated calves resided, and the remainder of the controls were selected from pens where no calves had been treated for UBRD. Due to the high treatment rates at both locations in 1985, the control calves constituted all of the nontreated animals; this amounted to 45 controls for the 48 treated calves at EBRC and 63 controls for the 71 treated calves at RCAT.

Statistical analysis

Cases of treated calves were included in the analysis if their data met the minimum criteria of having proper animal identification, drugs used, and complete data on response and relapse performance. In some instances, other data such as weights were missing. Because of the missing data, the number of cases available for use in analyses of different performance measures varied slightly.

All analyses were performed on an IBM mainframe computer using the Biomedical Data Package (BMDP), 1983 version.

Student's *t*-test was utilized to compare the arrival weights and subsequent weight gains of calves treated for UBRD to those of the nontreated controls. Treated calves were grouped into four different categories of therapy with respect to possible response and relapse status, and the average daily gain of each group was compared to that of the untreated controls using the *t*-test.

The *t*-test was also employed to compare responsive to nonresponsive and relapsing to nonrelapsing calves with respect to arrival weight, days to first treatment,

Table 4. Weight gain of calves treated for UBRD with various antimicrobials as first-line therapy (includes responsive and nonresponsive cases)

	Weight gain (kg/d)	
	First 28 days postarrival	Entire feeding period
Oxytetracycline		
mean ± SD	0.51 ± 0.55	1.12 ± 0.23
no. of observations	68	57
Penicillin		
mean ± SD	0.69 ± 0.52	1.15 ± 0.28
no. of observations	60	53
Trimethoprim-sulfadoxine		
mean ± SD	0.57 ± 0.49	1.11 ± 0.24
no. of observations	65	56

No significant differences ($p > 0.05$)

temperature at first treatment, and temperature at 48 hours after first treatment.

The response, relapse, and case fatality rates (calculated as risk rates) in the three antimicrobial treatment groups were compared using chi-square analysis. Analysis of variance (ANOVA) was used to compare the average daily gain of calves in each of these groups. Comparisons were carried out in two ways, the first using all calves started on a drug regardless of the outcome, and the second including only the responders.

Results

Rates of UBRD and response to treatment

The percentage of calves treated for UBRD ranged from 19.3% to 53.3% at the six different locations, with 34.6% of the 1179 calves observed receiving treatment for respiratory disease (Table 1). The response rate to first-line therapy ranged from 78.4–91.7% (Table 2). Relapse rates varied from 5–28.9%, and case fatality rates from 0–4%. Overall, the response, relapse, and case fatality rates were 85.7%, 14.8%, and 1.4% respectively.

There were six deaths, resulting in an overall mortality rate of 0.5% in the 1179 calves studied (Table 1). All mortality due to respiratory disease occurred during the first 28 days postarrival. There was one untreated mortality due to peracute fibrinous pneumonia (*Pasteurella haemolytica*) in a calf found dead 12 hours postarrival. One calf died as a result of acute interstitial pneumonia (no bronchopneumonia present) on the second day of oxytetracycline therapy. Two animals died of subacute fibrinous bronchopneumonia in combination with bovine virus diarrhea/mucosal disease; one of these had been started on penicillin and the other on trimethoprim-sulfadoxine. There were only two deaths due to uncomplicated fibrinous pneumonia, both of which occurred in trimethoprim-sulfadoxine treated calves on their second and third days of therapy. The calves had been started on treatment on days 5 and 7, respectively, postarrival. *Pasteurella multocida* was cultured from the lungs of both cases at autopsy.

Evaluation of three antimicrobials for therapy of UBRD

The response rates (Table 3) to the various antimicrobials were as follows: 86.2% for oxytetracycline, 87.8% for penicillin, and 83.3% for trimethoprim-sulfadoxine. These differences were not significant ($p > 0.10$). Relapse rates for those calves that responded to the first course of therapy (Table 3) were not significantly different ($p > 0.10$) at 13.2%, 14.0%, and 17.1% for oxytetracycline, penicillin, and trimethoprim-sulfadoxine, respectively. Similarly, case fatality rates for calves treated with each of the three antimicrobials were not significantly different (Table 3).

Weight gains of calves from EBRC and RCAT were examined for both the initial 28-day observation period and the entire feeding trial. When the average daily gain (ADG) of calves treated with the various antimicrobials was examined, no differences were noted (Table 4). Examination of the ADG of calves that exhibited a satisfactory response to first course of therapy with the respective drugs was also conducted. As evidenced in Table 5, no significant differences existed in either of the time periods examined.

Days to first treatment

Data on days to first treatment were available only at locations 3 to 6 (i.e. EBRC and RCAT in both years of the study). The average days to first treatment were 9.5 ± 5.3 (mean ± SD) on 203 calves with a range from day 0 postarrival to day 26. The median day of first treatment was day 10. The mean days to first treatment on the various arrival groups ranged from day 4.0 to day 11.5. Calves that did not respond to first-line antimicrobial therapy were treated at a mean of 8.4 days postarrival whereas responders were first treated at 9.7 days (Table 6). This difference was not statistically significant ($p > 0.10$). In contrast, calves that relapsed after their first course of therapy were first treated, on average, 6.1 days postarrival and nonrelapsing calves received first therapy at a mean of 10.1 days (Table 6). This difference in mean days to first treatment with respect to subsequent relapse status was significant ($p < 0.001$).

Arrival weights and weight gains

The relationship of treatment for UBRD to arrival weight and subsequent weight gain is presented in Table 7. Treated calves were lighter at arrival and gained significantly less ($p < 0.05$) than control calves during both of the time periods examined.

Although calves that responded and did not relapse (treated for a total of four days with a single antimicrobial) suffered from poor weight gains in the first month postarrival in comparison to the control calves ($p < 0.05$), this difference was not evident when the gains over the entire feeding period were analyzed (Table 8). Animals that responded but relapsed or were nonresponders that suffered no relapse had significantly ($p < 0.10$) impaired rates of gain over the total feeding period when compared to the nontreated controls (Table 8).

Table 5. Weight gain of calves treated for UBRD with various antimicrobials as first-line therapy (includes only responsive cases)

	Weight gain (kg/d)	
	First 28 days postarrival	Entire feeding period
Oxytetracycline		
mean ± SD	0.53 ± 0.51	1.14 ± 0.22
no. of observations	60	51
Penicillin		
mean ± SD	0.71 ± 0.53	1.14 ± 0.28
no. of observations	57	50
Trimethoprim-sulfadoxine		
mean ± SD	0.53 ± 0.47	1.12 ± 0.25
no. of observations	53	47

No significant differences ($p > 0.05$)

Discussion

Although the evaluation of a preventive or therapeutic procedure in a field trial is the next logical step after demonstrating efficacy under the controlled conditions of the laboratory, few trials are reported and, of those that are, few describe the experimental (study) population in sufficient detail to enable reliable extrapolation of results to a given reference (target) population. All experimental populations will not be equal with respect to the amount of morbidity nor the severity of disease due to UBRD. Likewise, therapeutic results will vary. Even in this study, with a single investigator overseeing a standardized case definition and assisting with detection of sick calves, response and relapse rates were quite variable between feedlots. Because of the low case fatality rates due to fibrinous pneumonia (5/360), this was the least variable outcome measured in the current trial. Feedlot operators and veterinarians have over the years come to accept that morbidity due to UBRD can be quite variable among groups and years within a single feedlot, but have at the same time been reluctant to accept variability in the performance of an antimicrobial without attempting to blame antimicrobial resistant strains of bacteria for the diversity of performance. Mechor *et al* (5) have recently documented that the outcome of therapy for UBRD has little relationship to the sensitivity pattern of *P. haemolytica* isolated on pretreatment nasal swabs. In the present study, the three antimicrobials performed similarly within a given feedlot. That is, there was greater variability in response, relapse, and case fatality rates among feedlots than among antimicrobials.

The design of this field trial was such that the primary outcome measure of interest was the response rate at 48 hours after first treatment with each of three antimicrobials. As such, it was necessary to obtain approximately 360 cases of UBRD, thereby allowing 120 calves to be treated with each of three different antimicrobials. This number of calves per treatment group is sufficient to declare a difference in response rates between two drugs as large as 15% (absolute change) or greater to be true, with the likelihood of type I and type II errors being 5% and 20%, respectively. A type I error occurs when it is declared that a treatment effect exists when in fact it does not. A type II error occurs when it is declared that no treatment effect exists when in fact the treatment does produce the specified effect (9).

The present study and the one by Mechor *et al* (5) demonstrate that the choice of first-line antimicrobial had no effect on response, relapse, or case fatality rates in two populations of feedlot calves that were derived from similar sources, but underwent different stresses with respect to distances transported and size of feedlot at destination. It would now seem germane to investigate detection strategies, nondetrimental ancillary therapies, or altered management during the period of therapy in order to alter therapeutic results. Investigation of "earlier" detection or more lenient case definition necessitates close scrutiny to balance them against "overtreatment" and its associated increase in costs.

The mean days to first treatment for calves in this study (9.5 days on 203 calves) is consistent with the patterns of treatment reported in other studies (3,4). On first examination, it is somewhat disappointing to find that the only predictor of a case that is likely to relapse is that it was treated at 6.0 days postarrival versus 10.1 days. However, the distribution of days to first treatment for relapsers is skewed to the left (towards day 0), making it feasible to consider such steps as extra days of therapy or the use of a convalescent pen for all animals treated in, for example, the first four days postarrival. In this study, 41% of the relapsers were treated before day 5 postarrival, whereas 17% of the nonrelapsers were treated in the same time period (data not shown). Thus, the chance of relapse (expressed as an odds ratio) is 3.5 times higher in a calf treated in the first four days postarrival than if treated after four days.

There exists some controversy as to the appropriate time after commencing treatment at which to make a decision regarding response to therapy for UBRD, and whether to make the decision on rectal temperature change, maintenance of temperature below a given point, or even whether temperature alone should be the deciding factor. Most statements on the subject are authoritarian rather than authoritative. Mechor *et al* (5) have recently noted that, in calves in which a subjective assessment was used to override a set temperature/time response criterion ($< 39.7°C$/48 hours), 45% of calves relapsed as opposed to 34% when the temperature/time standard alone was used to make the decision regarding response. In the present study, the assessment of response was totally objective, with a rectal temperature of $< 40°C$ at 48 hours being the sole criterion for a responder. This may seem somewhat at odds with the case definition which allowed calves to proceed to therapy at a temperature $\geq 39.5°C$ but was based on the fact that the cooperating feedlots were reluctant to forego beginning treatment on calves that satisfied all other criteria except that the temperature was between 39.4 and 40.0°C.

Thirty of the 363 calves (8.3%) started treatment at 39.5 to 39.9°C, inclusive. Some investigators argue that the case definition of acute UBRD should include only calves with temperatures $\geq 40.0°C$, but it is

Table 6. Treatment-related data based on response and relapse status

	Response		Nonresponse		Relapse		Nonrelapse	
	Mean ± SD	No. calves	Mean ± SD	No. calves	Mean ± SD	No. calves	Mean ± SD	No. calves
Arrival weight (kg)	227.3 ± 21.3	175	231.9 ± 21.0	28	233.0 ± 21.8	29	226.9 ± 20.8	172
Days to first treatment	9.7 ± 5.4	175	8.4 ± 4.8	28	6.1[a] ± 4.5	29	10.1[b] ± 5.3	172

[a,b]Significantly different, $p < 0.001$

Table 7. Relationship of arrival weight and subsequent weight gain to treatment for UBRD

	Arrival weight (kg)	Weight gain (kg/d)	
		First 28 days postarrival	Entire feeding period
Treated			
mean ± SD	228.0[a] ± 21.3	0.59[b] ± 0.52	1.12[c] ± 0.25
no. of observations	203	193	166
Control			
mean ± SD	235.1 ± 25.3	0.73 ± 0.51	1.18 ± 0.24
no. of observations	193	190	174

[a]Significantly different from control, $p < 0.01$
[b]Significantly different from control, $p < 0.01$
[c]Significantly different from control, $p < 0.05$

worthy of note that two of the five total case fatalities and one of the two case fatalities due to uncomplicated fibrinous pneumonia in this trial were started on treatment at < 40.0°C. It would appear that, in this population, it is probably cost effective to "overdiagnose" UBRD in order to reduce case fatalities. Low (< 40.0°C) temperatures at the start of therapy may indicate, as some authors suggest, that the animal is more advanced in the disease process (is a "late pull") or it could simply be that there is variability in the febrile response of the animal to different agents of UBRD.

The observation that treated calves were lighter and therefore likely younger than untreated animals is biologically plausible given that field observations for some time have shown that the older the calf, the less likely it is to develop UBRD (10). The explanation lies either in the fact that the larger calf is under less social stress in a group or has, through virtue of age, experienced active infection and the development of immunity to a greater number of agents of UBRD. It is also possible that the calves were lighter at arrival because they were subclinically ill and therefore not eating as well as the controls immediately upon arrival.

Numerous studies have monitored weight gain performance of calves treated for UBRD over short periods of time such as 28 days. Two studies that examined periods longer than 28 days (11,12) concluded that morbidity due to respiratory disease does not affect subsequent performance. It must be noted that, due to the small numbers of animals included in these studies, the power was lacking to detect differences if indeed they did exist. This has likely led to a large number of type II errors being committed. When large numbers of treated and control calves have been available (13,14), the results of the studies have been equally split. Cole *et al* (13) found that calves treated for BRD gained 0.12 kg/d less up to 56 days postarrival, but that when measured at day 149, ADG was not different due to compensatory gain among the treated calves. On the other hand, Hutcheson and Cole (14) concluded that although some compensatory gains occur after the first month, the treated animals are at a disadvantage compared to untreated controls over the remainder of the feeding period as well. The results obtained in the present study suggested a similar trend, with the calves treated for UBRD gaining 0.06 kg/d less than their untreated penmates over the total feeding period. Thus, treated calves could be as much as 11 kg lighter after a 180 day feeding period. This allows us to better define the economics of keeping calves healthy provided we retain the present case definition of UBRD. The present study is the first to look within the treated group to determine that both nonresponders that do not relapse and relapsers that initially responded suffer in terms of decreased average daily gain compared to treated animals that respond and do not relapse. Further studies are required to confirm these results in various populations of cattle and will require standardization of treatment protocols.

Although there is no significant difference in ADG of responding, nonrelapsing calves when compared to the untreated controls, the numerical difference of 0.03 kg/d bears further investigation in a study (of sufficient power) which has as its primary goal the definition of this as a real or chance difference. Documentation of differences such as these are essential for

Table 8. Weight gain of calves treated for UBRD based on response and relapse status to therapy

	Weight gain (kg/d)	
	First 28 days postarrival	Entire feeding period
Control		
mean ± SD	0.73 ± 0.51	1.18 ± 0.24
no. of observations	190	174
Respond, nonrelapse		
mean ± SD	0.63[a] ± 0.49	1.15 ± 0.25
no. of observations	147	128
Respond, relapse		
mean ± SD	0.35[b] ± 0.58	1.07[d] ± 0.23
no. of observations	23	20
Nonresponse, nonrelapse		
mean ± SD	0.66 ± 0.60	1.01[e] ± 0.23
no. of observations	21	17
Nonresponse, relapse		
mean ± SD	−0.23[c] ± 0.46	1.29 ± 0.00
no. of observations	2	1

[a]Significantly different from controls, $p < 0.05$
[b]Significantly different from controls, $p < 0.001$
[c]Significantly different from controls, $p < 0.01$
[d]Significantly different from controls, $p < 0.10$
[e]Significantly different from controls, $p < 0.01$

economic evaluation of feedlot health management strategies.

One of the major strengths of the current study rests with the fact that the study population was strongly representative of the reference population, namely calves weaned and transported to Ontario from western Canada in the fall of the year. The 19 different groups of calves from four provinces transported by truck and/or train to four feedlots over a period of two years represented literally hundreds of different farms and ranches of origin in western Canada. It should also be noted that all cases of UBRD occurring over the first 28 days at each lot were used. This avoids a possible bias that calves detected and entered onto a clinical trial over a short time period, such as two to three days, may not be representative of the entire population of treated calves to which we may wish to apply the results. As clinical trials become more prevalent in the veterinary literature, it will be useful for the authors to adequately consider and describe case definition, treatment protocol, and outcomes in the experimental populations, and to ensure that adequate numbers of experimental units are included in the trial to allow the detection of economically and biologically important differences.

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