The effect of respiratory disease and a preventative antibiotic treatment on growth, survival, age at first calving, and milk production of dairy heifers

A. L. Stanton,^{*1} D. F. Kelton,* S. J. LeBlanc,* J. Wormuth,† and K. E. Leslie*

^{*}Department of Population Medicine, University of Guelph, Guelph, Ontario, Canada N1G 2W1

[†]CY Heifer Farm, Batavia, NY 14020

ABSTRACT

Bovine respiratory disease complex (BRD) is a common disease in weaned dairy calves that incurs economic and welfare costs. This study was an extension of a randomized clinical trial in which a single injection of tulathromycin (TUL) or oxytetracycline (TET) was administered at first movement to group housing for the prevention of BRD in the 60 d following antimicrobial treatment (BRD60). Calves treated with TUL were 0.5 times [95% confidence interval (CI): 0.4 to 0.7] as likely to be treated for BRD60 as calves treated with TET. The objectives of the current study were to evaluate the long-term effects of BRD and antibiotic treatment on growth of heifers until breeding age, age at first calving, incidence of dystocia, milk production, and mortality before first calving and mortality before 120 d in milk. At entry to the breeding barn (382 d of age), calves that experienced BRD60 weighed 16.0 ± 2.3 kg less than calves that did not. Survival to first calving was recorded for 98% (1,343/1,392) of the heifers on this trial. For TET and TUL heifers with BRD60, 63% (94/150) and 73% (64/88) survived to first lactation, respectively. For TET and TUL calves without BRD60, 84% (436/517) and 84% (494/588) survived to first lactation, respectively. The median age at first calving for heifers with and without BRD60 was 714 (95% CI: 705–723) and 702 (95% CI: 699–705) days, respectively. Heifers with BRD60 were 1.5 (95% CI: 1.1–2.2) times more likely to have a calving ease score ≥ 2 at their first calving compared with heifers without BRD60. The administration of TUL at movement to group housing may have a role in the prevention of BRD and in mitigating some of the long-term effects of this disease. **Key words:** dairy heifer, bovine respiratory disease complex, growth, survival

INTRODUCTION

Bovine respiratory disease complex (BRD) is of concern due to the high economic and welfare costs associated with this condition. According to the 2007 US National Animal Health Monitoring Survey (NAHMS), the incidence of postweaning respiratory disease in dairy heifers was 5.9%, and it was the predominant cause of reported deaths of weaned heifers (46.5%; USDA, 2010). In cattle, BRD is a complex of disease processes most commonly resulting from infection with various microorganisms, including *Pasteurella multocida*, *Mannheimia haemolytica*, and *Mycoplasma* spp. The development of BRD is typically initiated by an environmental stressor and viral infection, which weaken the resistance mechanisms of the lungs and allow bacterial colonization of the lung (Yates, 1982). Common BRD prevention practices include vaccination, colostrum management, and good ventilation (Gorden and Plummer, 2010). This disease is often observed following the first movement to group housing after weaning (McGuirk, 2008). Risk factors for BRD include concurrent nutritional, environmental, and social changes, as well as increased exposure to pathogens from mixing with older animals for the first time.

Severe undetected or untreated BRD may result in death. Prompt therapy should result in a low case fatality risk, but this disease can represent an economic drain for producers. In the short term, the costs of this disease include labor for detection and treatment of disease, veterinary fees, reduced performance, and the cost to replace animals that die during clinical disease. Costs of this disease were estimated at \$14.71 (range: 0–\$119) per preweaned calf per year and \$1.95 (range: 0–\$9.25) per weaned dairy calf per year by Michigan producers in 1990 (Kaneene and Hurd, 1990). The long-term costs of BRD are likely underestimated due to the poor disease records that are often kept for heifers, which make it difficult for producers to associate calfhood BRD with long-term negative outcomes. Costs of long-term effects were estimated at between €18 and €57 (US\$15–\$49) in a partial budget of the cost of BRD on typical Dutch dairy farms, in which 60% of dairy

Received October 20, 2011.

Accepted May 8, 2012.

¹Corresponding author: astanton@uoguelph.ca

heifers were affected by mild to chronic BRD (van der Fels-Klerx et al., 2001). However, the effects of BRD on growth, survival, and production were based on a small number of studies examining these factors. These studies have documented different long-term costs, including increased risk of mortality before calving (Waltner-Toews et al., 1986), decreased growth (Virtala et al., 1996), later age at calving (Waltner-Toews et al., 1986; Correa et al., 1988), and increased risk of dystocia (Warnick et al., 1994). Warnick et al. (1995, 1997) found no association of calfhood BRD with first-lactation milk production or survival after first calving. However, calves with more than 4 treatments for BRD before calving were 2 times less likely to survive first lactation compared with calves with no BRD (Bach, 2011). Respiratory disease in beef feedlots is associated with decreased ADG, marbling, meat quality, and subcutaneous fat cover and increased mortality (Smith, 1998; Reinhardt et al., 2009; Schneider et al., 2009). These studies support the hypothesis that calfhood BRD has a negative effect on dairy heifer growth, age at first calving, dystocia, mortality, and milk production in first lactation. However, it is important to re-examine these effects over time because of changes in management practices, BRD treatments, and animal genetics.

The objectives of the present study were to evaluate the long-term effects of BRD and antimicrobial treatment on heifer performance. Specifically, we examined the growth rate of heifers until breeding, age at first calving, incidence of dystocia, milk production, and mortality before first calving and mortality before 120 DIM.

MATERIALS AND METHODS

This study is an extension of a randomized clinical trial in which a single injection of tulathromycin or oxytetracycline was administered to dairy heifers at first movement to group housing for the prevention of BRD in the 60 d following antimicrobial treatment (**BRD60**; Stanton et al., 2010). Briefly, 1,392 calves, raised in a commercial heifer-raising facility, were enrolled at first movement to group housing when they were 8 wk of age. In total, 248 calves were treated for BRD in the 60 d following enrollment. Calves assigned to the TUL group were 0.5 times (95% CI: 0.4 to 0.7) as likely to be treated for BRD in the 60 d following study enrollment than calves assigned to the TET group. This initial study was restricted to the first 60 d following movement to group housing.

Heifer Management and Housing

Heifers enrolled in this study (1,392) were reared at a commercial heifer-raising facility in western New York. They arrived at the facility from 7 separate source farms at (mean $\pm$ SD) 3 ± 2.1 d of age. Calves were enrolled following movement from individual housing in hutches or nursery barns during the milk-fed period to group housing after weaning. The average age at enrollment was 56 d. Calves were randomly assigned to either a subcutaneous injection of 200 mg of tulathromycin (**TUL**; Draxxin, Pfizer Animal Health, New York, NY) or an intramuscular injection of 1,000 mg of oxytetracycline (**TET**; Biomycin 200, Boehringer Ingelheim, St. Joseph, MO). The standard dose for TUL was determined based on the weight of the upper quartile of calves (78 kg) at enrollment. The dose of TET was part of the established weaning management protocol on the farm and was two-thirds of a full label dose. During the study, no antibiotics were administered in the feed or water.

Calves were monitored for disease for 60 d following study enrollment. The definition of BRD was dullness, decreased appetite, or listlessness, with at least one of the following signs: a rectal temperature $>39.5^{\circ}\text{C}$, nasal discharge, or elevated respiratory effort. Respiratory disease was diagnosed in 13.2% (92/697) of TUL calves and in 22.4% (156/695) of TET calves during the 60 d following first movement to group housing (Stanton et al., 2010).

All heifers were housed in a bedded-pack barn (weaning barn) with a scrape alley for the first 6 wk following movement to group housing. Following the first movement to group housing, heifers were moved through an additional 4 barns (transition barn, grower barn 1, grower barn 2, and breeding barn). After the weaning barn, all heifers were housed in naturally ventilated freestalls until they left the heifer-raising facility.

All heifers remained at the facility until they were confirmed pregnant. After confirmation of pregnancy, heifers were eligible to return to their source farm and did so based on the preset preferences of the original source farm. All heifers were returned to their original source farms unless they died or were culled before calving.

Outcome Measures

BW, Height, and ADG. All calves were monitored daily in the nursery, weaning, and transition barns by trained staff for the occurrence of disease, using consistent case definitions. All disease events and

treatments were recorded in the farm management database (DairyComp 305, Valley Agricultural Software Inc., Tulare, CA). When heifers were returned to their source farms to calve and enter the milking herd, all subsequent disease, production, calving, and mortality information was recorded by the farms' staff using DairyComp 305.

Weights and heights of calves were measured at standard times using an electronic scale (Tru-Test ID3000, Tru-Test Inc., Mineral Wells, TX) as part of the standard operating procedure of the commercial heifer-rearing facility. Height at the withers (to the nearest inch) was measured at the same time as weight. Measurements were taken at entry into the nursery barn (mean $\pm$ SD; age, 3 ± 2 d), weaning barn (56 ± 7 d), transition barn (98 ± 8 d), grower barn 1 (181 ± 13 d), grower barn 2 (269 ± 31 d) and breeding barn (382 ± 33 d). For simplicity, these measures will now be referred to as occurring at 0, 2, 3, 6, 9, and 13 mo of age.

Survival, Age at First Calving, Dystocia, and Milk Production. One of the source farms on this trial had limited on-farm records. For this reason, heifers on this farm were not followed past their removal from the heifer-raising facility and were not included in analysis of survival, age at calving, dystocia, or milk production. This source farm accounted for 3% (48/1,392) of calves from the original database.

Survival to first calving was deemed to occur if heifers calved in their original source herd. Survival to 120 DIM was deemed to occur if heifers were present in their source herd for ≥ 120 d after their first calving.

Median and quartile values were presented for age at first calving because the data set was not normally distributed. The outcome age at first calving was divided into heifers that calved up to and including 25 mo of age and those that calved after 25 mo of age. This cut-point was based on the widely used economic target of a calving age of 24 mo with an additional month added to allow for heifers to calve within their 24th month (Le Cozler et al., 2008).

Calving ease was scored with the standard 5-point scale of the DHIA as part of the source farms' standard practices. Calving ease scores were defined as follows: 1 = no problem, 2 = slight problem, 3 = needed assistance, 4 = considerable force, and 5 = extreme difficulty. Cut-points of calving ease scores ≥ 2 , ≥ 3 , ≥ 4 , and 5 were independently assessed as potential indicators of dystocia because no validated cut-point exists for dystocia.

Regular DHIA milk testing was performed at monthly intervals on 4 of the 6 farms and every other month on the remaining farms. First test milk production and third test projected 305-d milk production were col-

lected for the 4 farms using monthly testing. First test milk production and second test projected 305-d milk production were collected for the 2 farms that were testing every other month in an attempt to standardize DIM at test-days among the 6 farms.

Culling and Mortality. The causes of culling and mortality were entered into DairyComp305 by the staff of the heifer-raising facility or of the individual source farms, depending on the location of the animal at the time the determination was made. Producer-attributed cause of death was recorded as respiratory disease, injury, other, or unknown. Culling was divided into the following categories based on the primary reason given by producers: respiratory, other diseases, sold for dairy, failure to conceive, injury, poor growth, or other.

Statistical Analysis

All analyses were conducted using SAS version 9.1 (SAS Institute Inc., Cary, NC). Enrollment season was offered to all models as a fixed effect. Season was divided into 3 periods based on a visual assessment of daily temperature recordings obtained from the Rochester, New York, weather station (approximately 65 km from the heifer-raising facility; Underground Weather, 2010): moderate [$5 \pm 4^\circ\text{C}$ (mean $\pm$ SD); November 1, 2006, to January 15, 2007]; cold ($-2 \pm 7^\circ\text{C}$; January 16 to April 15, 2007); or warm ($18 \pm 6^\circ\text{C}$; April 16, 2007, to the end of the trial in July 2007).

BW, Height, and ADG. The effects of BRD60 and antimicrobial treatment on BW, height, and ADG were evaluated at each management time point, corresponding to entry into successive barns at 0, 2, 3, 6, 9, and 13 mo of age. Body weight, height, and ADG were evaluated using linear regression mixed models (PROC MIXED) with random effects for source farm and weekly enrollment cohort. The models for BW controlled for birth weight, pre-enrollment ADG (pADG), pre-enrollment respiratory disease (pBRD), season, and age at measurement. The models of height controlled for height at birth, pBRD, season, and age at measurement. The models of ADG controlled for birth weight, pBRD, pADG, enrollment season, and age of the animal at their final measurement.

Dystocia, Survival to First Calving, and First-Lactation Survival (120 d). The dichotomous outcomes survival to first calving, age category at first calving, dystocia at various cut-points, and first-lactation survival to 120 d following calving were analyzed using mixed models with binary distribution and logit link function (Proc GLIMMIX). Source farm and weekly enrollment cohort were included as random effects. Antimicrobial treatment, BRD60, pBRD, and enrollment season were included as fixed effects.

Table 1. Descriptive results of the age, weight, and height of Holstein calves at entry into the 6 rearing barns at a commercial heifer-raising facility (mean $\pm$ SD) and number of heifers with or without bovine respiratory disease in the 60 d following movement to group housing (BRD60+ or BRD60–, respectively) and heifers that received tulathromycin (TUL) or oxytetracycline (TET) at movement to group housing at entry into 6 rearing barns

Variable	Rearing barn					
	Nursery barn	Weaning barn	Transition barn	Grower barn 1	Grower barn 2	Breeding barn
Total animals (no.)	1,392	1,392	1,373	1,333	1,301	1,271
Age (d)	3 $\pm$ 2	56 $\pm$ 7	98 $\pm$ 9	181 $\pm$ 13	270 $\pm$ 34	382 $\pm$ 33
BW (kg)	40 $\pm$ 5	71 $\pm$ 11	109 $\pm$ 16	190 $\pm$ 27	273 $\pm$ 41	370 $\pm$ 39
Height (cm)	80 $\pm$ 3	90 $\pm$ 4	98 $\pm$ 4	109 $\pm$ 4	118 $\pm$ 4	127 $\pm$ 3
BRD60+ (no.)	248	248	240	213	207	199
BRD60– (no.)	1,144	1,144	1,133	1,120	1,094	1,072
TUL (no.)	698	698	690	670	652	640
TET (no.)	694	694	683	663	649	631
Death before entry ¹	—	—	29	58	90	119
Missing weights (no.)	0	0	0	1	1	2

¹Animals that died between enrollment (entry into the weaning barn) and before entering the rearing barn. No deaths were recorded before entry into the nursery or weaning barns as heifers were not enrolled on this trial until the day they were moved to the weaning barn.

To determine if the animals with the most severe cases of BRD were removed before first calving, the interaction between BRD60 and survival to first calving was tested for an association with ADG between 2 and 3 mo of age. Average daily gain between 2 and 3 mo was chosen as a surrogate for disease severity as it was assumed that the most severely affected animals would have the lowest weight gain during clinical disease, which occurred primarily during this time period. Average daily gain was modeled using a linear mixed model (PROC MIXED) with random effects for source farm and weekly enrollment cohort. The model controlled for birth weight, pBRD, pADG, season, and age of the animal at their final measurement.

Age at First Calving. The effect of BRD60 and antimicrobial treatment on time to first calving was analyzed using a Cox proportional hazard survival analysis model (PROC Phreg), stratified by source farm, and a nonparametric estimate of the survival distribution function (PROC Lifetest).

Milk Production. First DHIA test milk weight and 305-d projected milk production were analyzed using linear regression mixed models (PROC MIXED) with random effects for source farm, weekly enrollment cohort, and calving season. Calving season was divided into 4 categories based on the month heifers calved: spring (March 1 to May 31), summer (June 1 to August 31), fall (September 1 to November 30), and winter (December 1 to February 28). These models evaluated the effect of BRD60 and antimicrobial treatment on milk production controlling for DIM at DHIA testing and age at first calving as fixed effects. Residual diagnostics and normality were assessed using Proc Univariate.

Exclusion Criteria. One source farm did not provide records after return to the farm for calving. This

source farm accounted for 3% (48/1,392) of calves from the original database. These calves were included in analysis of ADG. However, animals from this farm were excluded from analysis of survival to first calving and from analyses of all events that occurred after calving.

RESULTS

The average age, BW, and height of calves at each measurement time point, corresponding to entry into new rearing barns at the facility, are presented in Table 1.

ADG

Effects of BRD60 on ADG are presented in Table 2. Overall, BRD60 was associated with reduced ADG between 2 and 9 mo. An antimicrobial treatment and pBRD interaction was significant between 2 and 6 mo of age (Table 2). After 6 mo, antimicrobial treatment and pBRD had no effect on ADG ($P > 0.05$).

BW

Heifers with BRD60 weighed 7.1 ± 0.6 , 11.4 ± 1.4 , 15.4 ± 1.8 , and 14.4 ± 2.17 kg less at 3, 6, 9, and 13 mo compared with heifers without BRD60 ($P < 0.001$). An interaction between antimicrobial treatment and pBRD interactions was significant for all weights after 3 mo of age ($P < 0.05$). For calves with no pBRD, TUL calves weighed 4.1 ± 0.5 , 5.9 ± 1.4 , 6.1 ± 1.4 , and 5.3 ± 1.7 kg more than TET calves at 3, 6, 9, and 13 mo of age ($P < 0.001$). For calves with pBRD, antimicrobial treatment had no effect on BW ($P = 0.77, 0.48, 0.67$, and 0.8 at 3, 6, 9 and 13 mo, respectively).

Table 2. Linear regression of the ADG of heifers (estimates $\pm$ SE; *P*-values in parentheses) from approximately 2 to 13 mo of age recorded during housing in 4 barns with random effects for source farm and weekly enrollment cohort

Variable ¹	Between 2 and 3 mo	Between 3 and 6 mo	Between 6 and 9 mo	Between 9 and 13 mo
Number	1,373	1,332	1,300	1,269
Intercept	0.70 $\pm$ 0.11 (<0.001)	0.37 $\pm$ 0.11 (0.01)	0.91 $\pm$ 0.07 (<0.001)	1.25 $\pm$ 0.08 (0.07)
BRD60+ (Referent = BRD60-)	-0.17 $\pm$ 0.01 (<0.001)	-0.07 $\pm$ 0.02 (<0.001)	-0.04 $\pm$ 0.01 (0.001)	(0.83)
Antimicrobial treatment $\times$ pBRD	(0.002)	(0.05)	(0.59)	(0.28)
TUL with pBRD	-0.01 $\pm$ 0.02 (0.90)	-0.03 $\pm$ 0.02 (0.15)		
TUL without pBRD	0.10 $\pm$ 0.01 (<0.001)	0.02 $\pm$ 0.01 (0.07)		
TET with pBRD	-0.01 $\pm$ 0.02 (0.79)	0.01 $\pm$ 0.02 (0.74)		
(Referent = TET without pBRD)	0	0		
TUL (Referent = TET)			(0.53)	(0.96)
pBRD (Referent = no pBRD)			(0.91)	(0.08)
Season	(0.006)	(0.002)	(0.01)	(<0.001)
Moderate	0.10 $\pm$ 0.03 (0.006)	-0.07 $\pm$ 0.02 (0.002)	-0.05 $\pm$ 0.03 (0.09)	-0.05 $\pm$ 0.03 (0.09)
Warm	0.04 $\pm$ 0.03 (0.15)	0.01 $\pm$ 0.02 (0.76)	-0.08 $\pm$ 0.03 (0.004)	0.06 $\pm$ 0.02 (0.01)
Cold	Referent	Referent	Referent	Referent
Birth weight ² (kg)	0.002 $\pm$ 0.001 (<0.001)	0.004 $\pm$ 0.001 (<0.001)	0.004 $\pm$ 0.001 (<0.001)	0.002 $\pm$ 0.01 (0.02)
ADG between 0 and 2 mo (kg/d)	0.34 $\pm$ 0.05 (<0.001)	0.12 $\pm$ 0.05 (0.01)	(0.81)	(0.28)
Age at outcome measurement (d)	(0.14)	0.002 $\pm$ 0.001 (<0.001)	-0.0004 $\pm$ 0.0002 (0.06)	-0.001 $\pm$ 0.001 (<0.001)

¹BRD60- = no clinical bovine respiratory disease complex in the 60 d following enrollment; BRD60+ = treated for clinical bovine respiratory disease complex in the 60 d following enrollment; pBRD = treated for clinical bovine respiratory disease complex between arrival at the heifer-raising facility (± 3 d) and enrollment on the trial (± 56 d); TUL = calves randomly assigned to treatment with tulathromycin upon movement to group housing at 2 mo of age; TET = calves randomly assigned to treatment with oxytetracycline upon movement to group housing at 2 mo of age.

²Birth weight was measured upon arrival at the heifer-raising facility, which occurred, on average, at 3 d of age.

Height

Calves treated for BRD60 were 1.7 ± 0.4 cm smaller than calves without BRD60 when measured at 13 mo of age ($P < 0.001$). At 6 mo, we observed an interaction of the effects of antimicrobial treatment and pBRD ($P = 0.0009$; Table 3). The TUL calves were 0.6 ± 0.2 taller than the TET calves at 9 mo of age, regardless of pBRD status ($P < 0.001$).

Survival to First Calving

One heifer returned to her source farm but was lost to follow-up before calving. Heifers from one source farm ($n = 48$) were removed from analysis due to poor records on the source farm. In total, 1,343 of 1,392 heifers had complete records until death or first calving. This represented 96% (238/248) of the BRD60+ heifers and 97% (1,105/1,444) of the BRD60- heifers.

In total, 1,088/1,343 (81%) heifers survived to first calving at their source farms. Only 66% (158/238) of calves with BRD60 survived to first calving compared with 84% (931/1,105) of calves without BRD60 that survived to first calving. Survival to first calving was 83% (559/676) and 79% (530/667) for TUL and TET calves, respectively. Of the 237 calves with BRD60, 73% (64/88) of the TUL calves survived to first calving and 62% (93/149) of the TET calves survived to first calving.

Survival to first calving was affected by BRD60 and antimicrobial treatment with a significant interaction between antimicrobial treatment and BRD60 ($P < 0.03$). For TET and TUL, the odds of survival to first calving among calves without BRD60 were 3.4 (95% CI: 2.2 to 5.2) and 1.7 (95% CI: 1.0 to 2.9) times greater than that of calves with BRD60, respectively. Among calves treated for BRD60, the odds of survival to first calving were 2.0 (95% CI: 1.1 to 3.6) times greater if

Table 3. Differences of least squares means ($\pm$ SE; *P*-values in parentheses) in wither height (cm) between heifers administered tulathromycin (TUL) or oxytetracycline (TET) at first movement to group housing (2 mo) and between heifers with and without bovine respiratory disease in the 60 d following first movement to group housing (BRD60) at a commercial heifer-raising facility¹

Variable	3 mo	6 mo	9 mo	13 mo
BRD60 vs. no BRD60	-1.3 ± 0.2 (<0.001)	-1.9 ± 0.02 (<0.001)	-1.6 ± 0.2 (<0.001)	-1.7 ± 0.4 (<0.001)
TUL vs. TET	0.4 ± 0.1 (0.003)		0.6 ± 0.2 (<0.001)	(0.13)
pBRD vs. no pBRD	-1.2 ± 0.2 (<0.001)		-1.0 ± 0.3 (<0.001)	-0.6 ± 0.2 (0.008)
Antimicrobial treatment $\times$ pBRD	(0.08)	(0.009)	(0.61)	(0.07)
TUL with pBRD		-1.0 ± 0.2 (<0.001)		
TUL with no pBRD		0.9 ± 0.2 (<0.001)		
TET with pBRD		0.5 ± 0.4 (0.18)		
TET with no pBRD		Referent		

¹The linear mixed model controlled for age at final measurement, bovine respiratory disease before trial enrollment (pBRD), height at birth, season, with random effects for source farm and weekly enrollment cohort.

they had received TUL at movement to group housing compared with TET. Antimicrobial treatment did not have an effect on the probability of calves without BRD60 surviving to first calving ($P = 0.80$).

The association between survival and growth between 2 and 3 mo of age was assessed for 1,325 animals. This analysis excluded all heifers from one source farm due to incomplete records ($n = 48$) and an additional 19 heifers from the remaining 6 source farms that died before their weight was measured at 3 mo of age. The interaction between survival to first lactation and BRD60 was significantly associated with ADG between 2 and 3 mo of age ($P < 0.001$). For heifers with BRD60+, the ADG of heifers that were culled before first lactation was 0.18 ± 0.03 kg lower than the ADG of heifers that survived to first lactation ($P < 0.001$). For heifers with BRD60–, the ADG of heifers that were culled before first lactation was 0.06 ± 0.02 kg less than that of heifers that survived to first lactation ($P < 0.01$). For heifers that survived to first lactation, the ADG of BRD60+ heifers was 0.15 ± 0.02 kg less than that of BRD60– heifers.

Table 4. Producers' primary reasons for the 7% (93/1,343) of heifers that died between enrollment (8 wk of age) and calving

Producer-attributed cause of death	Proportion of total deaths, % (no./no.)
Respiratory disease	47 (44/93)
Injury	27 (25/93)
Nonrespiratory diseases	14 (13/93)
Other	1 (1/93)
Unknown	11 (10/93)

Culling and Mortality Before First Calving

Of the 255 heifers that did not survive to first calving, 36% (93/255) died and 64% (162/255) were culled. The primary reason for mortality was BRD, with 47% (44/93) of all deaths attributed to this disease (Table 4). For the deaths attributed to BRD, 61% (27/44) were treated for BRD in the 60 d following movement to group housing. Failure to conceive was the primary reason stated for culling of heifers (Table 5).

Age at First Calving

Of the 1,088 heifers that returned to calve at their source farms, the median age at first calving was 703 (first and third quartile; 683 to 737) d. The median age at first calving was 714 (first and third quartile; 705–723) and 702 (699 to 706) d for BRD60+ and BRD60– calves, respectively. Based on the results of a Cox survival analysis, heifers with BRD60 were 0.8 (95% CI: 0.7 to 1.0) times as likely to calve as heifers without BRD60 stratified by source farm ($P = 0.02$;

Table 5. Producers' primary reason for the 12% (162/1,343) of heifers removed (alive) between enrollment (8 wk of age) and calving

Primary reason for culling	Proportion of cullings, % (no./no.)
Failure to conceive	32 (51/162)
Poor growth	22 (36/162)
Dairy	22 (35/162)
Nonrespiratory diseases	16 (26/162)
Injury	4 (6/162)
Bovine respiratory disease complex	2 (3/162)
Other or unknown	3 (5/162)

Figure 1. Time to event analysis for age at first calving in 248 heifers that had respiratory disease between 2 and 4 mo of age (BRD60+) and 1,144 heifers that did not (BRD60–; $P = 0.02$).

Figure 1). Antimicrobial treatment was not significant in this model ($P = 0.11$).

Only 19% (205/1,088) of heifers failed to calve before 25 mo of age. The proportion of BRD60+ and BRD60– heifers that failed to calve before 25 mo of age was 27% (43/158) and 17% (162/931), respectively. Controlling for source farm, enrollment cohort, and antimicrobial treatment, the odds of calving by 25 mo of age were 0.6 (95% CI: 0.4 to 0.8) times lower in calves with BRD60 ($P = 0.01$). We found no association ($P = 0.98$) of antimicrobial treatment with probability of calving by 25 mo of age.

Dystocia

Calving ease scores were recorded for 98% (1,066/1,088) of heifers that calved at their source farms (Table 6). Fifty-five percent of the heifers with BRD60 had a calving ease score ≥ 2 (85/155) compared with 46% (424/911) of calves without BRD60. Controlling for source farm, enrollment cohort and antimicrobial treatment, calves with BRD60 were 1.5 (95% CI: 1.1 to 2.2) times more likely to have a calving ease score ≥ 2 at their first calving than calves without BRD60 ($P = 0.03$). However, BRD60 was not associated with the probability of calving scores ≥ 3 (Table 7). We found no association of antimicrobial treatment with the probability of a calving score ≥ 2 , ≥ 3 , or ≥ 4 ($P = 0.71$, $P = 0.98$, and $P = 0.18$, respectively).

Milk Production

First Test-Day Milk Production. Of the 1,088 heifers with DairyComp records who calved on the source farm, 13 had milk samples collected too early in the lactation (<10 d) for accurate estimates to be recorded, and 5 heifers had health problems that affected the milk sample quality. An additional 3 heifers did not have their first milk test records recorded in their DairyComp file for unknown reasons. Prior to the collection of their first milk test, 23 heifers died or were sold. In total, 1,044 heifers had first DHIA test milk production data.

First test milk production tended to be 1.1 ± 0.6 kg lower for heifers with BRD60 than for BRD60– heifers, controlling for DIM and age at calving as random effects and source farm and calving season as fixed effects ($P = 0.06$). Antimicrobial treatment and pBRD were not significant in this model ($P = 0.24$ and $P = 0.15$, respectively).

Table 6. Distribution of calving ease score recorded by source farms

Score	Definition	Proportion, % (no./no.)
1	No problem	52 (557/1,066)
2	Slight problem	24 (259/1,066)
3	Needed assistance	14 (151/1,066)
4	Considerable force	6 (60/1,066)
5	Extreme difficulty	4 (39/1,066)

Table 7. The association of respiratory disease between 2 and 4 mo of age and ease of first calving as evaluated in a logistic model with random effects for source farm and enrollment cohort¹

Calving ease score/definition	Incidence of dystocia events, % (no./no.)		Odds ratio [95% CI]	P-value
	BRD60+	BRD60–		
2+: Slight problem or greater	55 (85/155)	46 (424/911)	1.5 [1.1–2.2]	0.03
3+: Needed assistance or greater	27 (42/155)	23 (208/911)	1.3 [0.9–2.0]	0.17
4+: Considerable force or greater	11 (17/155)	9 (82/911)	1.4 [0.8–2.5]	0.32
5: Extreme difficulty	5 (7/155)	4 (32/911)	1.4 [0.6–3.4]	0.44

¹BRD60+ = treated for clinical bovine respiratory disease complex in the 60 d following enrollment; BRD60– = no clinical bovine respiratory disease complex in the 60 d following enrollment.

Projected 305-d Milk Production. Of the 1,088 heifers that calved with complete records on the source farm, 12 heifers were still in their original source farm herd but did not have the required samples for projected 305-d milk production at the time of study completion. Fifty-seven heifers died or were sold between calving and collection of the milk sample required for projected 305-d milk production. In total, 1,019 heifers had complete records for projected 305-d milk production.

For every day that age at first calving increased, projected 305-d milk production decreased by 2.8 ± 1.3 (LSM $\pm$ SEM) kg, controlling for DIM as a fixed effect and source farm, weekly enrollment, and calving season as random effects ($P = 0.04$). Bovine respiratory disease in the 60 d following movement to group housing (BRD60) and antimicrobial treatment were not significantly associated with 305-d milk production ($P = 0.48$ and $P = 0.50$, respectively).

Survival to 120 DIM

Twenty-four of the 1,088 heifers that calved (2%) were still on their original source farm but were less than 120 DIM at the time of analysis. Complete records were available for 1,064 heifers for survival to 120 DIM. For the heifers with complete records, 94% (1,001/1,064) survived to 120 DIM. Neither BRD60 nor antimicrobial treatment significantly affected survival to 120 DIM controlling for source farm, enrollment cohort, and calving season as random effects ($P = 0.39$ and $P = 0.40$, respectively).

DISCUSSION

This study evaluated the long-term effects of BRD under modern management conditions and the long-term effects of a novel approach to reducing the incidence of BRD in dairy calves. Specifically, the effect of a long-acting prophylactic treatment was compared with a shorter acting prophylactic treatment. Respiratory disease has previously been documented to have long-term effects on the health and productivity of

dairy heifers (Virtala et al., 1996; Donovan et al., 1998). However, these studies have become dated or may not reflect current North American management practices.

The negative effects of BRD60 on ADG following movement to group housing were seen until approximately 9 mo of age, or 7 mo after movement to group housing. This difference in ADG resulted in a 14.3 ± 2.1 kg decrease in BW for calves with BRD60 at approximately 13 mo of age. This is consistent with previous studies reporting that the number of days treated for BRD before 6 mo of age decreased ADG between 6 and 14 mo by 0.02 kg/d (Donovan et al., 1998). However, direct comparison is not possible given the variation in follow-up time and the differences in outcomes. Donovan et al. (1998) looked at number of days treated, whereas this study assessed the presence or absence of a BRD event within the first 60 d of movement to group housing. The results of the current study and those of Donovan et al. (1998) and Virtala et al. (1996) indicate that BRD has a negative effect on the growth of dairy heifers for many months after initial treatment. This is inconsistent with findings from the beef feedlot industry that BRD following arrival and processing at a feedlot does not have a significant long-term effect on ADG following an initial clinical phase (Thompson et al., 2006; Holland et al., 2010). This discrepancy may be due to differences in the stage of the animal's physical development at onset of disease, or a difference in the type or incidence of pathogens. In the study by Holland et al. (2010), beef animals entered the study at 241 kg and they contracted respiratory disease in the preconditioning phase, which occurred over the next 63 d. Following the preconditioning phase, no effect of BRD treatment on ADG was observed. The disparity in size between the calves on the present study (enrolled at 71 kg) may indicate that the age and weight of the animal at disease onset play a role in the effect of BRD.

Bovine respiratory disease in the 60 d following first movement to group housing was associated with a lower shoulder height (by 1.1 ± 0.2 cm) at 13 mo of age. The maximum observed difference in height between heifers with and without a recorded case of BRD60 was

-1.9 ± 0.2 cm at approximately 180 d of age. This is consistent with the findings of Donovan et al. (1998) that the effect of BRD on height gain is primarily seen in the first 6 mo of life. However, as shown in this study, the effect on delayed growth in stature can remain up to 1 yr of life.

For calves without BRD before enrollment, calves treated with TUL at first movement to group housing had a 0.10 ± 0.01 and 0.02 ± 0.01 kg increase in ADG until approximately 6 mo of age compared with calves treated with TET. This suggests that TUL had a short-term effect on the ADG of dairy calves in calves with no history of BRD before antimicrobial treatment. This incremental increase in BW was maintained until 13 mo of age. For heifers with a history of BRD before enrollment, antimicrobial treatment had no effect on growth. This absence of antimicrobial treatment effect in calves with a prior history of BRD indicates that antimicrobial treatment does not compensate for an earlier disease occurrence, likely due to the effect BRD has already had on heifer health and performance. This indicates that treatment with TUL is most beneficial for animals with no history of BRD before movement to group housing and is housed in a population that is at risk of BRD in the period immediately following movement to group housing.

It should be noted that the comparison between antimicrobial treatments is limited by the discrepancies in dosages. The dosage of TET was based on the previously established farm protocol of the commercial heifer-raising facility. Calculation of the dosage of TET that would be appropriate based on the weights of calves in this study indicates that the dose of TET used was lower than optimal. As such, different effects might be expected with a full dose (Stanton et al., 2010).

Respiratory disease following movement to group housing had a negative effect on the survival of heifers to first calving. A reduction in survival to first calving has 2 main effects on the productivity of a farm. It reduces the ability of producers to make genetic gains by reducing the pool of animals from which to select and retain replacements. Furthermore, several indirect costs incurred for heifers that die, including the loss of the future value of the cow, the wasted costs associated with rearing the animal up to its death, and the cost of purchasing a replacement for the lost heifer if heifers are needed for the lactating herd. As shown in this study, heifers with BRD60+ were 1.7 to 3.4 times more likely to be removed from the herd before first calving for the TUL and TET group, respectively. This is consistent with the findings of Waltner-Toews et al. (1986), who found that heifers treated for BRD in the first 90 d of life were 2.5 times more likely to die between 90 d of age and calving. These 2 studies differ from Curtis et

al. (1988), who found that respiratory disease was not associated with survival to calving. These differences may be due to the severity of the disease events considered. Curtis et al. (1988) included any BRD event regardless of treatment, whereas both this study and Waltner-Toews et al. (1986) included only calves that were ill enough to be treated.

Calves treated for BRD60 had 2.0 (95% CI: 1.1 to 3.6) times higher odds of survival to first calving if they had received TUL at movement to group housing compared with TET (i.e., before disease occurrence). A possible explanation for this interaction is that the longer duration of activity of TUL relative to TET may have reduced the severity of the infection of BRD60 in some calves. The comparison between these 2 groups must be made cautiously because the lack of a true positive control in this trial. However, further study is warranted on the effect of TUL administered around weaning on the survival of calves that developed BRD based on these results.

Age at first calving is an important factor for producers because it has a significant effect on the lifetime productivity of heifers (Le Cozler et al., 2008). Warnick et al. (1994) found that heifers with BRD in the first 3 mo of life calved 3 mo later than heifers without BRD. The present study found that heifers treated for BRD in the 60 d following movement to group housing were almost half as likely to calve before 25 mo (odds ratio: 0.6; CI: 0.4 to 0.8) than heifers without BRD. Waltner-Toews et al. (1986) found no effect of BRD on the probability of calving by 30 mo of age, using a sample size approximately half that of the present study. This difference may also be explained by changes in dairy herd management between the United States and Canada as well as industry-wide changes since the 1980s related to selection for lower age at first calving and genetic selection for health and production traits, such as calving ease and increased milk production.

Dystocia is an important issue in the dairy industry. According to the 2007 NAHMS report, difficulty in calving occurred in 18% of heifers (USDA, 2009). Dystocia is most common in heifers and is commonly associated with BW at calving, age at calving, and sex of the calf (Mee, 2008). In addition, calves born from dystocia events are more likely to be stillborn. Difficulty in calving is associated with decreased reproductive performance (Mee, 2008). Dystocia can increase the risk of retained placenta and displaced abomasum (Correa et al., 1993; Laven and Peters, 1996). Defining dystocia is challenging and subject to interpretation. In this study, various cut-points were used on a standardized scale of calving ease scores to assess the effect of BRD on dystocia. Respiratory disease did not significantly affect dystocia rates if the calving ease score was

≥ 3 . However, the small number of animals with calving ease scores ≥ 3 limits the power to draw inferences. In this study, calves with BRD60 were 1.5 (95% CI: 1.1 to 2.2) times more likely to have at least mild dystocia (calving ease score ≥ 2). This is lower than in Warnick et al. (1994), who found that calves with BRD were 2.4 times more likely to have dystocia, but does add support to the association of calfhood respiratory disease with dystocia.

Bovine respiratory disease in the 60 d following movement to group housing tended to decrease first test milk weight by 1.1 ± 0.6 kg and had no effect on projected 305-d milk production. The results from 305-d milk production are consistent with a previous study that found no long-term effects of BRD following entry into milk production (Warnick et al., 1995). This may be due to many factors, including culling of low producers, a high level of variation in the estimate of 305-d milk production, and the large number of factors that influence longer term milk production. In addition, the use of the second or third milk test estimate of 305-d milk production is less accurate than full-lactation milk production, which may have affected the association with BRD60.

Among heifers that calved, BRD60 did not affect survival to 120 DIM. This could be due to many factors, including prior selection for healthy animals, such that by the time animals have calved, the most severely affected animals had been removed from the herd. Further culling may occur after 120 d and bears further examination.

It is worth noting that the effects of BRD on dystocia, milk production, and postcalving survival may be underestimated because the most severely affected animals have already been removed before first lactation. This culling represents a survival bias and is a common challenge in long-term studies of diseases. Although we cannot directly measure the effect of survival, the findings that heifers with BRD60+ were more likely to be culled before first calving and had the lowest ADG does support the theory that survival bias occurred in this study. The results of this study support that BRD60 decreases calving ease and has a tendency to affect first test milk production. However, it was not possible to measure these outcomes in heifers that were culled. With this in mind, the results of this study are most likely representative of heifers with mild to moderate BRD, as the most severe cases were removed before calving. Future studies of BRD should attempt to measure the severity of BRD during clinical disease to better quantify the survival bias. This may result in a more accurate measure of the effect of BRD severity on survival, calving ease, and milk production.

CONCLUSIONS

Treatment with TUL was associated with higher growth rates for approximately 4 mo after treatment in calves without prior BRD. This effect is likely a result of a reduced incidence of subclinical disease in the first 60 d following movement to group housing. In addition, TUL treatment at first movement to group housing may be associated with a reduction in the severity of clinical disease based on the increased survival to first calving among calves with BRD60. Respiratory disease in the first 60 d following movement to group housing decreased growth, decreased survival to first calving, increased age at first calving, decreased calving ease, and (among heifers that survived to first lactation) tended to have an equivocal short-term effect on first milk test production.

ACKNOWLEDGMENTS

The authors acknowledge Suzanne T. Millman (Veterinary Diagnostic and Production Animal Medicine & Biomedical Science, Iowa State University, Ames) and Tina M. Widowski (Department of Animal & Poultry Science, University of Guelph, Guelph, ON, Canada), the staff and management of CY Heifer Farms (Elba, NY) and participating source farms for their invaluable contribution to this research. Funding was provided by Pfizer Animal Health (New York, NY) and the National Science and Engineering Research Council of Canada (Ottawa, ON, Canada).

REFERENCES

- Bach, A. 2011. Associations between several aspects of heifer development and dairy cow survivability to second lactation. *J. Dairy Sci.* 94:1052–1057.
- Correa, M. T., C. R. Curtis, H. N. Erb, and M. E. White. 1988. Effect of calfhood morbidity on age at first calving in New York herds. *Prev. Vet. Med.* 6:253–262.
- Correa, M. T., H. Erb, and J. Scarlett. 1993. Path analysis for seven postpartum disorders of Holstein cows. *J. Dairy Sci.* 76:1305–1312.
- Curtis, C. R., J. M. Scarlett, H. N. Erb, and M. E. White. 1988. Path model of individual-calf risk factors for calfhood morbidity and mortality in New York Holstein herds. *Prev. Vet. Med.* 6:43–62.
- Donovan, G. A., I. R. Dohoo, D. M. Montgomery, and F. L. Bennett. 1998. Calf and disease factors affecting growth in female Holstein calves in Florida, USA. *Prev. Vet. Med.* 33:1–10.
- Gorden, P. J., and P. Plummer. 2010. Control, management, and prevention of bovine respiratory disease in dairy calves and cows. *Vet. Clin. North Am. Food Anim. Pract.* 26:243–259.
- Holland, B. P., L. O. Burciaga-Robles, D. L. VanOverbeke, J. N. Shook, D. L. Step, C. J. Richards, and C. R. Krehbiel. 2010. Effect of bovine respiratory disease during preconditioning on subsequent feedlot performance, carcass characteristics, and beef attributes. *J. Anim. Sci.* 88:2486–2499.
- Kaneene, J. B., and H. S. Hurd. 1990. The national animal health monitoring system in Michigan. III. Cost estimates of selected dairy cattle diseases. *Prev. Vet. Med.* 8:127–140.

- Laven, R. A., and A. R. Peters. 1996. Bovine retained placenta: Aetiology, pathogenesis and economic loss. *Vet. Rec.* 139:465–471.
- Le Cozler, Y., V. Lollivier, P. Lacasse, and C. Disenhaus. 2008. Rearing strategy and optimizing first-calving targets in dairy heifers: A review. *Animal* 2:1393–1404.
- McGuirk, S. M. 2008. Disease management of dairy calves and heifers. *Vet. Clin. Food. Anim.* 24:139–153.
- Mee, J. F. 2008. Prevalence and risk factors for dystocia in dairy cattle: A review. *Vet. J.* 176:93–101.
- Reinhardt, C. D., W. D. Busby, and L. R. Corah. 2009. Relationship of various incoming cattle traits with feedlot performance and carcass traits. *J. Anim. Sci.* 87:3030–3042.
- Schneider, M. J., R. G. Tait Jr., W. D. Busby, and J. M. Reecy. 2009. An evaluation of bovine respiratory disease complex in feedlot cattle: Impact on performance and carcass traits using treatment records and lung lesion scores. *J. Anim. Sci.* 87:1821–1827.
- Smith, R. A. 1998. Impact of disease on feedlot performance: A review. *J. Anim. Sci.* 76:272–274.
- Stanton, A. L., D. F. Kelton, S. J. LeBlanc, S. T. Millman, J. Wormuth, R. T. Dingwell, and K. E. Leslie. 2010. The effect of treatment with long-acting antibiotic at postweaning movement on respiratory disease and on growth in commercial dairy calves. *J. Dairy Sci.* 93:574–581.
- Thompson, P. N., A. Stone, and W. A. Schultheiss. 2006. Use of treatment records and lung lesion scoring to estimate the effect of respiratory disease on growth during early and late finishing periods in South African feedlot cattle. *J. Anim. Sci.* 84:488–498.
- Underground Weather. 2010. Historical records from Rochester New York Weather Station. Accessed Jun. 22, 2012. <http://www.wunderground.com/history/airport/KROC/2009/1/19/MonthlyHistory.html>.
- USDA-APHIS (US Department of Agriculture-Animal and Plant Health Inspection Service). 2009. Dairy 2007, Part IV: Reference of dairy cattle health and management practices in the United States, 2007. USDA-APHIS-VS-CEAH, Fort Collins, CO. Accessed Jun. 1, 2012. http://www.aphis.usda.gov/animal_health/nahms/dairy/downloads/dairy07/Dairy07_dr_PartIV.pdf.
- USDA-APHIS (US Department of Agriculture-Animal and Plant Health Inspection Service). 2010. Dairy 2007, Heifer calf health and management practices on U.S. dairy operations, 2007. USDA-APHIS-VS-CEAH, Fort Collins, CO. Accessed Jun. 1, 2012. http://www.aphis.usda.gov/animal_health/nahms/dairy/downloads/dairy07/Dairy07_ir_CalfHealth.pdf.
- van der Fels-Klerx, H. J., J. T. Sorensen, A. W. Jalvingh, and R. B. Huirne. 2001. An economic model to calculate farm-specific losses due to bovine respiratory disease in dairy heifers. *Prev. Vet. Med.* 51:75–94.
- Virtala, A. M. K., G. D. Mechor, and Y. T. Grohn. 1996. The effect of calfhoo diseases on growth of female dairy calves during the first 3 months of life in New York State. *J. Dairy Sci.* 79:1040–1049.
- Waltner-Toews, D., S. W. Martin, and A. H. Meek. 1986. The effect of early calfhoo health status on survivorship and age at first calving. *Can. J. Vet. Res.* 50:314–317.
- Warnick, L. D., H. N. Erb, and M. E. White. 1994. The association of calfhoo morbidity with first-lactation calving age and dystocia in New York Holstein herds. *Kenya Vet.* 18:177–179.
- Warnick, L. D., H. N. Erb, and M. E. White. 1995. Lack of association between calf morbidity and subsequent first lactation milk production in 25 New York Holstein herds. *J. Dairy Sci.* 78:2819–2830.
- Warnick, L. D., H. N. Erb, and M. E. White. 1997. The relationship of calfhoo morbidity with survival after calving in 25 New York Holstein herds. *Prev. Vet. Med.* 31:263–273.
- Yates, W. D. 1982. A review of infectious bovine rhinotracheitis, shipping fever pneumonia and viral-bacterial synergism in respiratory disease of cattle. *Can. J. Comp. Med.* 46:225–263.