Case-control study to determine herd-level risk factors for bovine respiratory disease in nursing beef calves on cow-calf operations

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OBJECTIVE
To determine herd-level risk factors for bovine respiratory disease (BRD) in nursing beef calves.

DESIGN
Matched case-control study.

SAMPLE
84 cow-calf operations in Nebraska, North Dakota, and South Dakota.

PROCEDURES
Case herds were herds that treated at least 5% of the calf crop for BRD prior to weaning. Control herds were herds that treated < 0.5% of the calf crop for BRD prior to weaning. Each case herd was matched with 2 control herds on the basis of veterinary practice and enrollment year. Herd owners or managers were interviewed by telephone, and characteristics and practices associated with case status were determined by multivariable conditional logistic regression.

RESULTS
30 case herds and 54 control herds were evaluated. Increasing herd size, frequent pasture movement for intensive grass management (intensive grazing), and use of estrus-synchronization programs were significantly associated with herd status. The odds of being a case herd for herds with 150 to 499 cows was 7.9 times and that for herds with ≥ 500 cows was 12 times, compared with the odds of being a case herd for herds with < 150 cows. The odds of being a case herd for herds that used intensive grazing was 3.3 times that for herds that did not use intensive grazing. The odds of being a case herd for herds that used an estrus-synchronization program was 4.5 times that for herds that did not use an estrus-synchronization program.

CONCLUSIONS AND CLINICAL RELEVANCE
Management practices can be associated with an increase in the BRD incidence in nursing beef calves. Modification of management practices may decrease BRD incidence in nursing calves for herds in which it is a problem. (*J Am Vet Med Assoc* 2018;252:989–994)

Surveys conducted by the USDA indicate that BRD is the leading cause of death in US feedlot cattle,[1] weaned dairy heifers,[2] and nursing beef calves ≥ 3 weeks old.[3] Unlike feedlot cattle and dairy calves, little research has been conducted to characterize risk factors for BRD in nursing beef calves. Bovine respiratory disease in nursing calves has been reported in approximately 20% of US beef cow-calf herds,[4,5] and a 2014 analysis estimates that BRD in nursing calves costs US cow-calf producers $259.4 million annually.[a] Thus, BRD in nursing calves represents an important source of loss for some cow-calf producers, but the lack of published research on risk factors for BRD in nursing calves makes it difficult for veterinarians to make evidence-based decisions regarding practices to minimize the disease on affected operations.

ABBREVIATIONS
BRD Bovine respiratory disease

Some information regarding risk factors associated with BRD in nursing calves has been gleaned from surveys of cow-calf producers. Analysis of data collected by the USDA National Animal Health Monitoring System indicated that the incidence of BRD in nursing calves was greater in herds consisting of crossbred or composite cattle, compared with herds consisting of purebred cattle, and in herds that are the primary source of income for the producer, import weaned steers, feed calves antimicrobials to control BRD, or allowed visitors.[6] Results of a producer survey[5] conducted by our research group indicated that the odds of identifying at least 1 nursing calf with BRD were greater in cow-calf herds that had diarrhea in calves, had treated at least 1 cow for BRD, or for herds located in Plains states (but not Eastern states), had a calving season that lasted ≥ 3 months. Additionally, the proportion of nursing calves treated for BRD was greater in herds that bring in orphan or grafted calves from outside sources, have ≥ 50% of calves born between Janu-

ary and April, creep feed nursing calves, or use estrus-synchronization programs.[5] Thus, it appears that some management practices and herd characteristics likely increase the risk for BRD in nursing calves, and such factors may be amenable to manipulation to decrease the disease in affected herds.

The purpose of the study reported here was to increase the body of information regarding risk factors for BRD in nursing calves. The strength of data obtained by surveys is limited by factors such as low response rates. Therefore, we designed a matched case-control study to evaluate herd-level risk factors for BRD in nursing calves on cow-calf operations in 3 states (Nebraska, North Dakota, and South Dakota). Anecdotal reports indicated that cow-calf producers and veterinarians in those states had a fairly high level of interest in BRD in nursing calves, which we believed would facilitate recruitment of an adequate number of herds for the study.

Materials and Methods

Herd identification and enrollment

Prior to study initiation, it was anticipated that approximately 20 to 30 case herds would be available for enrollment. An a priori sample size calculation was performed as described[7] with the following assumptions: type I error probability of 10%, power of 80%, exposure prevalence of 50% in control herds, correlation of 0.2 between each case herd and its matched controls, and a clinically relevant OR of 4 with a 2-tailed alternative hypothesis. Results indicated that the necessary sample size was 25 case herds, each with 2 matched control herds.

Information regarding the study was distributed to national and state veterinary and producer organizations during the summers of 2012, 2013, and 2014 to identify case herds. To be eligible for study enrollment, herds had to be located in Nebraska, North Dakota, or South Dakota; have a mean calf weaning age of ≥ 120 days; and have at least 30 cows calve during the spring of the enrollment year. Case herds were defined as herds that treated a minimum of 5% of nursing calves for BRD or, for herds with < 80 calves born per year, treated at least 4 nursing calves for BRD. Prospective case herds were confirmed to have treated the required number of nursing calves for BRD by the consulting or herd veterinarians. Control herds were defined as herds with < 400 calves that treated ≤ 1 nursing calf for BRD or herds with ≥ 400 calves that treated ≤ 0.5% of nursing calves for BRD during the study enrollment year.

Herd participation in the study was voluntary. The intention was to match each case herd with 2 control herds on the basis of veterinary practice and enrollment year whenever possible. The veterinary practice that provided service to each case herd was identified. Then, all other cow-calf operations serviced by that practice were enumerated on a list, and a computerized random number generator was used to randomly select herds until 2 control herds for each case herd were identified or the list was exhausted.

Telephone interviews

One of 4 senior investigators (ARW, DRS, RFD, or GLS) conducted a brief telephone interview with the manager or owner of each prospective study herd to obtain information on the incidence of BRD in nursing calves and determine whether the herd met the criteria for either a case or control herd. In the fall or winter of the enrollment year (ie, after calves were weaned), 1 of 3 investigators (TA, ATD, or MJ) conducted a second, longer telephone interview (**Supplementary Appendix S1**, available at avmajournals.avma.org/doi/suppl/10.2460/javma.252.8.989) with the manager or owner of each participating herd to obtain detailed information regarding operation characteristics and management practices. The first and second (management survey) interviews were conducted by different groups of investigators to ensure that the investigators who conducted the management survey were unaware of the case or control status of the participating herds. The University of Georgia Human Subjects Office evaluated both surveys and determined that they did not require full review by the Institutional Review Board.

The management survey was designed to determine whether cows and calves were managed in > 1 group; cattle were frequently moved to different pastures to intensively manage grass (intensive grazing); cattle had fence-line contact with other herds; cows or calves were provided any supplemental feed; any bulls, replacement heifers, adult cows, orphan or grafted calves, stocker or backgrounding cattle, or feedlot cattle were added to the herd from outside sources (ie, herd was open); an estrus-synchronization program was used for cows or heifers during the year of the survey; cattle were screened for bovine viral diarrhea virus; or cows and calves were ever herded or walked > 1.6 km (1 mile). Other information collected during the survey included the duration of the calving season, mean age and weight of calves at weaning, incidence of calf diarrhea, whether cows or calves were administered respiratory vaccines, and whether any adult cows or heifers were treated for BRD.

Statistical methods

Conditional logistic regression was used to evaluate herd-level risk factors for BRD in nursing calves while accounting for the matched case-control study design. For all models, the outcome was modeled as the probability that the herd was a case herd. Initially, univariable analyses were conducted to determine which predictor variables were associated with the case-control status of the herds. Predictor variables with a value of $P < 0.20$ on univariable analysis were eligible for inclusion in a multivariable model. Selection of the multivariable model was performed with a maximum main-effects procedure in which all eligible variables were included in the model and then manually removed on the basis of their level of significance (ie, P value) in a step-wise manner until only variables with values of $P < 0.10$ remained. Herd size was retained in all models regardless of its significance because it was considered an important confound-

ing variable. After determination of the preliminary main-effects multivariable model, the significance of all previously removed variables was reevaluated and all possible 2-way interactions between main-effects were evaluated in that model. All analyses were performed with commercially available software[b] with the assumption of a 2-sided alternative hypothesis. Because there is currently no commercially available software program that can calculate residuals and influence statistics for a conditional logistic regression model with n:m (eg, 1:2) matching, residual analysis of the final model was not performed.

Results

Herds

Thirty case herds and 54 control herds were enrolled in the study. Of the 84 herds evaluated, 52

Table 1—Characteristics for 84 beef cow-calf operations located in Nebraska, North Dakota, and South Dakota that did (case herds; n = 30) or did not (control herds; 54) treat a substantial proportion of nursing calves for BRD during the year of enrollment.

Variable	Control herds	Case herds
No. of primiparous and multiparous cows that calved during enrollment year	173 (40–1,490)	325 (80–930)
Proportion of the herd composed of primiparous cows (%)	12.8 (0.0–30.0)	15.0 (0.0–25.0)
Length of the calving season (d)	93 (37–218)	95 (36–259)
Proportion of calves that survived from 48 h old until weaning (%)	99.1 (92.0–100)	98.1 (90.2–100)
Mean calf age at weaning (d)	183 (150–260)	180 (120–245)
Mean calf weight at weaning (kg)	249 (170–345)	256 (181–352)
Proportion of calves treated for BRD before weaning (%)	0.0 (0.0–1.6)	20.2 (5.1–100)
Proportion of calves that died from BRD before weaning (%)	0.0 (0.0–1.6)	0.7 (0.0–7.8)

Values represent the median (range). Case herds were defined as herds that treated at least 5% of the calf crop for BRD prior to weaning. Control herds were defined as herds that treated < 0.5% of the calf crop for BRD prior to weaning. Of the 84 herds evaluated, 52 were enrolled in 2012, 24 were enrolled in 2013, and 8 were enrolled in 2014. Twenty-nine herds were located in Nebraska, 23 herds were located in North Dakota, and 32 herds were located in South Dakota.

Table 2—Results of univariable regression analyses to identify herd-level variables associated with BRD in nursing calves for the cow-calf herds of Table 1.

Variable	Control herds	Case herds	Matched OR (90% confidence interval)	*P* value*
No. of primiparous and multiparous cows calving				0.013
< 150	25 (46.3)	3 (10)	Referent	—
150–499	18 (33.3)	18 (60)	9.7 (2.6–36)	0.004
≥ 500	11 (20.4)	9 (30)	12 (2.4–60)	0.010
Were cow-calf pairs separated by calf age?				
No	38 (70.4)	12 (40)	Referent	—
Yes	16 (29.6)	18 (60)	4.1 (1.7–10)	0.009
Were cattle moved to different pastures for intensive grazing?				
No	26 (48.1)	6 (20)	Referent	—
Yes	28 (51.9)	24 (80)	3.4 (1.4–8.2)	0.021
Did cows undergo an estrus-synchronization program after calving?				
No	47 (87)	19 (63.3)	Referent	—
Yes	7 (13)	11 (36.7)	4.9 (1.9–13)	0.007
Were any cattle tested for bovine viral diarrhea virus?				
No	51 (94.4)	25 (83.3)	Referent	—
Yes	3 (5.6)	5 (16.7)	5.8 (1.2–28)	0.065
Were cows and calves herded or walked > 1.6 km at any time prior to weaning?				
No	19 (35.2)	7 (23.3)	Referent	—
Yes	35 (64.8)	23 (76.7)	2.2 (0.8–5.8)	0.186
Were primiparous cows kept in a confined area for calving?				
No	11 (20.4)	2 (6.7)	Referent	—
Yes	43 (79.6)	28 (93.3)	3.2 (0.85–12)	0.151
Did any calves die from diarrhea (scours)?				
No	44 (81.5)	18 (60)	Referent	—
Yes	10 (18.5)	12 (40)	3.1 (1.2–7.9)	0.046
Were any cattle treated for BRD?				
No	49 (90.7)	21 (70)	Referent	—
Yes	5 (9.3)	9 (30)	4.1 (1.5–11)	0.020

Values represent the number (percentage) of herds unless specified otherwise.

*Wald *P* value for univariable conditional logistic regression model, in which the outcome was modeled as the probability of being a case herd (ie, herds that treated a minimum of 5% of nursing calves for BRD or, for herds with < 80 calves born, treated at least 4 nursing calves for BRD). Variables with values of $P < 0.20$ were eligible for inclusion in a multivariable conditional logistic regression model.

— = Not applicable.

See Table 1 for remainder of key.

were enrolled in 2012, 24 were enrolled in 2013, and 8 were enrolled in 2014. Each herd was enrolled in the study only once (ie, a herd enrolled in 2012 was not reenrolled in 2013 or 2014). Twenty-nine herds were located in Nebraska, 23 herds were located in North Dakota, and 32 herds were located in South Dakota. A total of 18 matched sets of case and control herds were enrolled from 17 veterinary practices; 16 practices contributed matched sets during a single year of the study, and 1 practice contributed matched sets during 2 years. Within each matched set, the number of case herds ranged from 1 to 4 and the number of control herds ranged from 1 to 10 such that there was a mean of 1.8 control herds for each case herd. Characteristics of the enrolled herds were summarized **(Table 1)**.

Risk factors for BRD in nursing calves

Results of univariable conditional logistic regression analyses indicated that the following herd-level risk factors were associated ($P < 0.20$) with a herd being classified as a case herd: increasing herd size, separation of cow-calf pairs by calf age, use of intensive grazing, use of an estrus-synchronization program after calving, testing cattle for bovine viral diarrhea virus, herding or walking cattle for > 1.6 km at any time prior to weaning, calving primiparous cows in a confined area, calf deaths attributed to diarrhea, and treating adult cows for BRD **(Table 2)**. Herd-level variables not associated with a herd being classified as a case herd included number of groups in which cattle were managed, having fence-line contact with other cattle operations, supplemental feeding of cows or calves, addition of cattle from outside sources to the herd, checking cows for pregnancy, duration of calving season, mean age and weight of calves at weaning, and administration of respiratory vaccines to cows or calves.

The final multivariable conditional logistic regression model included herd size, use of intensive grazing, and use of an estrus-synchronization program after calving **(Table 3)**. The odds of being a case herd for herds with 150 to 499 cows was 7.9 times and that for herds with ≥ 500 cows was 12 times, compared with the odds of being a case herd for herds with < 150 cows. Herds that used intensive grazing were 3.3 times as likely to be classified as a case herd, compared with herds that did not use intensive grazing. Finally, herds that used an estrus-synchronization program after calving were 4.5 times as likely to be classified as a case herd, compared with herds that did not use an estrus-synchronization program after calving.

Discussion

Similar to other surveys of beef cow-calf producers,[5,6] results of the present matched case-control study identified specific herd characteristics and management practices that were significantly associated with BRD in nursing calves. Importantly, increasing herd size and the use of an estrus-synchronization program after calving were significantly associated with BRD in nursing calves in both the present case-control study and previous survey[5] of cow-calf producers in 6 US states. The herds evaluated in the present study were located in Nebraska, North Dakota, and South Dakota, whereas the herds evaluated in the previous survey[5] were located in 3 Eastern states (Florida, Georgia, and West Virginia) and 3 Plains states (Iowa, Kansas, and Nebraska); thus, the herds represented in the 2 studies were generally located in different states. However, the definition of BRD in nursing calves used to assess risk factors differed between the previous survey[5] and present study. In the previous survey,[5] factors associated with a producer identifying at least 1 nursing calf with BRD or with the proportion of calves treated for BRD were evaluated, whereas in the present study, factors associated with at least 5% of nursing calves being treated for BRD (ie, case herd) were evaluated. The fact that increasing herd size and use of an estrus-synchronization program after calving were identified as significant risk factors in both the previous survey[5] and present study, despite differences in the design of the 2 studies, increases the likelihood that those factors are truly associated with BRD in nursing calves. Interestingly, in another

Table 3—Results of multivariable regression analysis to identify herd-level variables associated with BRD in nursing calves for the cow-calf herds of Table 1.

Variable	Regression coefficient (SE)	Matched OR (90% confidence interval)	*P* value*
No. of primiparous and multiparous cows calving			0.034
< 150	Referent	—	—
150–499	2.07 (0.84)	7.9 (2.0–31)	0.014
≥ 500	2.46 (1.09)	12 (2.0–70)	0.024
Were cattle moved to different pastures for intensive grazing?			
No	Referent	—	—
Yes	1.20 (0.62)	3.3 (1.2–9.2)	0.051
Did cows undergo an estrus-synchronization program after calving?			
No	Referent	—	—
Yes	1.51 (0.67)	4.5 (1.5–14)	0.024

*Wald *P* value for multivariable conditional logistic regression model, in which outcome was modeled as the probability of being a case herd.

See Tables 1 and 2 for remainder of key.

study,[6] herd size was not significantly associated with the incidence of BRD in nursing calves, although the incidence of BRD in nursing calves in herds in which cattle were considered the primary income source for producers was greater than that in herds in which cattle were not the primary income source for producers, and cattle as a primary income source could have been a proxy for herd size.

In the present study, frequent movement of cattle to different pastures for intensive management of grass (intensive grazing) was associated with BRD in nursing calves. In the previously described survey,[5] producers were not specifically asked whether they used intensive grazing, but they were asked whether cow-calf pairs were rotated through multiple pastures before the calves were weaned, and movement through multiple pastures was not retained in the final multivariable model. Perhaps intensive grazing is a more important risk factor for BRD in nursing calves in the states (Nebraska, North Dakota, and South Dakota) where the herds of the present study were located than in the states (Florida, Georgia, Iowa, Kansas, Nebraska, and West Virginia) where the herds of the previous survey[5] were located.

The positive association between herd size and incidence of BRD in nursing calves might be attributable to factors that are truly causative. It is possible that large cow-calf herds have as yet unidentified characteristics that increase the risk of BRD for nursing calves. Alternatively, large herds may be at an increased risk for BRD in nursing calves simply because they have more susceptible calves than small herds, or large herd producers or managers spend more time observing calves and are more likely to identify calves with BRD than small herd producers or managers.

The design of the present study did not allow us to determine why use of an estrus-synchronization program after calving and use of intensive grazing were associated with BRD in nursing calves. It is possible both practices may increase the opportunity for effective contact between calves or between cows and calves. An effective contact is an interaction between an individual shedding an infectious agent and an individual that is susceptible to infection with that agent, which results in infection of the susceptible individual. Many estrus-synchronization programs require cows to undergo 2 to 3 treatments during a period of 1 to 2 weeks, and generally calves are temporarily separated from their dams and placed in a holding pen while the cows are treated. Thus, calves are separated from their dams and commingled closely with other calves on more than 1 occasion during a short period of time, both of which can be stressful and may impair immune system function. Moreover, it increases the amount of close contact among calves, which can facilitate transmission of infectious pathogens within the group. Notably, estrus-synchronization programs are generally implemented to shorten the calving season, resulting in groups of calves with a fairly narrow age range the subsequent year. Also, estrus-synchronization programs are typically initiated when the current calf crop is approximately 90 to 120 days old, a period during which the maternal antibodies passively acquired by those calves have begun to decline substantially. Results of another study[8] indicate that, in cow-calf herds that have a problem with BRD in nursing calves, most calves become affected between 100 and 150 days old, which is consistent with the hypothesis that nursing calves are at greatest risk for BRD after passively acquired maternal antibodies have decayed. Consequently, estrus synchronization of cows may increase the risk of BRD for nursing calves because it generally results in groups of calves with a fairly narrow age range and is associated with the comingling of those calves in a manner that increases the number of effective contacts during a period when many calves have lost maternal antibody protection. Assuming that hypothesis is true, BRD in nursing calves within herds that also use estrus-synchronization programs might be mitigated by either improving the immunity of calves (eg, respiratory vaccine administration) prior to comingling or comingling calves for the first time at a young age (ie, < 90 days old) so they can have effective contacts when they are at less risk of developing disease owing to the presence of maternal antibodies. Anecdotally, veterinarians suggest that the holding areas where calves are comingled while their dams are undergoing treatment for estrus synchronization are often poorly shaded and dusty without easy access to water, all of which may exacerbate the susceptibility of calves to respiratory tract infection. Similar to estrus-synchronization programs, intensive grazing can increase the frequency of close contact between cows and calves, resulting in an increased risk for BRD when calves become susceptible owing to the natural decay of maternal antibodies.

Although use of an estrus-synchronization program was positively associated with the risk of BRD in nursing calves in both the present study and previous survey,[5] it is worth noting that only 18 of the 84 (21%; 11 case herds and 7 control herds) herds evaluated in the present study used an estrus-synchronization program. Thus, other risk factors not identified as significant in the present study are likely to be important in some herds, and failure to identify those factors may have been due, in part, to the fairly small number of herds enrolled in this study. Factors significantly associated with the prevalence of BRD in nursing calves in other studies, such as feeding calves antimicrobials for the prevention of BRD[6] or in a creep feeder,[5] might increase the risk of BRD by increasing the frequency of effective contacts. Collectively, those findings suggest that, in herds in which BRD in nursing calves is a problem, the disease might be mitigated by the prevention of close contact between calves, particularly when calves are between 90 and 150 days old and have not had the opportunity to develop adequate active immunity to replace lost maternal immunity, or by facilitating the resistance of calves to respiratory tract infection by the use of relevant respiratory vaccines prior to comingling. Further research is necessary to confirm whether such practices would indeed be beneficial.

Unlike previous surveys, practices that facilitate the introduction of novel pathogens to a herd, such as the introduction of weaned steers[6] or orphan calves,[5] were not significantly associated with the risk of BRD in nursing calves in the present study. Although such practices may merit control in herds in which BRD in nursing calves is a problem, failure to identify a significant association between those practices and BRD in nursing calves in the present study might simply be an indication that outside sources of infection are less likely to contribute to BRD in nursing calves in cow-calf operations in Nebraska, North Dakota, and South Dakota than in cow-calf operations in other regions.

Even though the present study provided relevant new information regarding risk factors for BRD in nursing calves on US cow-calf operations, it was not without limitations. Those limitations included evaluation of a small number of herds from a fairly restricted geographic region. Thus, important risk factors for BRD in nursing calves in other regions of the United States or in other countries may not have been identified in this study. Further research to characterize risk factors for BRD in nursing calves in other regions is warranted as is research to determine whether modification of practices associated with estrus synchronization or intensive grazing can decrease the incidence of BRD in nursing calves in cow-calf operations that engage in those practices. Because estrus-synchronization programs and intensive grazing are progressive practices that might have an overall net benefit for cow-calf producers, it seems efforts to identify modifications that might mitigate the incidence of BRD in nursing calves in herds where it is a problem would be preferable to discouraging the use of those practices entirely.

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Footnotes

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