

Prevalence, outcome, and health consequences associated with persistent infection with bovine viral diarrhea virus in feedlot cattle

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Objective—To estimate prevalence of cattle persistently infected (PI) with bovine viral diarrhea virus (BVDV) at arrival at a feedlot, prevalence of chronically ill and dead PI cattle, and the magnitude of excess disease attributable to a PI animal.

Design—Cross-sectional and cohort studies.

Animals—2,000 cattle at the time they arrived at a feedlot, 1,383 chronically ill cattle from 7 feedlots, and 1,585 dead cattle from a single feedlot.

Procedure—Skin biopsy specimens were collected and evaluated via immunohistochemistry. Cattle were characterized as either PI or not PI with BVDV on the basis of characteristic immunostaining. Follow-up was obtained for the 2,000 cattle from which samples were collected at arrival, and health outcomes were determined for cattle exposed and not exposed to a PI animal.

Results—Prevalence of PI cattle was 0.3% at arrival, 2.6% in chronically ill cattle, and 2.5% in dead cattle. Risk of initial treatment for respiratory tract disease was 43% greater in cattle exposed to a PI animal, compared with those not exposed to a PI animal. Overall, 15.9% of initial respiratory tract disease events were attributable to exposure to a PI animal.

Conclusions and Clinical Relevance—Relatively few PI cattle arrive at feedlots. However, those cattle are more likely to require treatment for respiratory tract disease and either become chronically ill or die than cattle that are not PI. In addition, they are associated with an increase in the incidence of respiratory tract disease of in-contact cattle. (*J Am Vet Med Assoc* 2005;226:595–601)

Bovine viral diarrhea virus (BVDV) is an important pathogen of cattle and infection can lead to a variety of adverse health outcomes such as enteritis, abortion, fetal malformation, and bovine respiratory tract disease (BRD). The latter is by far the most important cause of increased rates of morbidity and mortality in feedlot cattle.^{1,2} Bovine viral diarrhea virus may contribute to the pathogenesis of BRD either as a primary respiratory pathogen or through immunosuppres-

sion.^{3,4} Ultimately, BVDV acts synergistically with other respiratory pathogens^{5,6} to facilitate bacterial colonization of the lower portion of the respiratory tract, which may give rise to fibrinonecrotic bronchopneumonia, the underlying lesion of BRD.

The feedlot industry invests considerable time and money in prevention of BVDV-induced disease. Most feedlot cattle in the United States are administered a BVDV-containing vaccine on feedlot arrival,⁷ although well-controlled vaccine efficacy studies conducted in real-world settings are generally lacking. In a recent study,¹ the authors reported that a tetravalent vaccine economically reduced morbidity rate in feedlot cattle, compared with a univalent vaccine; however, it could not be determined from their study whether the observed benefit was derived from the inclusion of BVDV or from other viral antigens or their combination.

Because cattle persistently infected (PI) with BVDV shed large quantities of the virus,^{8,9} they are presumably an important source of BVDV exposure for in-contact cattle. It seems plausible that identification and removal of these cattle could be included as part of a comprehensive BVDV control program. However, little is known concerning the prevalence and outcomes of PI cattle entering feedlots or if the presence of 1 or more PI cattle results in a detectable increase in the frequency of adverse health events for in-contact cattle. Ultimately, although it is generally accepted that BVDV results in disease in feedlot cattle, no estimate is available regarding the proportion of disease events attributable to BVDV or contact with a PI animal. These estimates are required to determine the economic burden of BVDV to the feedlot industry and to evaluate the cost effectiveness of control programs.

The advent of a sensitive and specific diagnostic test to detect PI cattle by use of immunohistochemical techniques on formalin-fixed skin biopsy specimens affords the opportunity to study the epidemiologic features of PI cattle in feedlots.^{10,11} The objectives of the study reported here were to estimate the prevalence of cattle PI with BVDV at feedlot arrival, the prevalence of chronically ill and dead PI cattle, and the magnitude of excess disease attributable to the presence of a PI animal.

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Materials and Methods

Cattle—Skin biopsy specimens were collected from 3 groups of cattle and histologically evaluated for specific immunohistochemical staining patterns characteristic of a persistent BVDV infection.¹⁰ The 3 groups of cattle included new arrivals at a single feedlot (group 1), chronically ill cattle derived from 7 feedlots (group 2), and a census of dead cattle during a 12-month period at a single feedlot (group 3). The feedlots used to house cattle for groups 1 and 3 were also sources of cattle for group 2. Cattle used in these studies were housed in or derived from 7 commercial feedlots located in southwest Kansas (n = 2) and the Texas Panhandle (5); group 2 cattle were housed in a feedlot for convalescent cattle, which was also located in the Texas Panhandle.

Group 1—Cross-sectional and cohort studies were performed with 2,000 auction market-derived, light yearling steers. Upon arrival, the cattle were administered doramectin (200 µg/kg [91 µg/lb]),^a a multivalent clostridial toxoid,^b and a vaccine^c containing live variants of bovine herpesvirus type 1, parainfluenza virus type 3, BVDV (types 1 and 2), and bovine respiratory syncytial virus. In addition, a growth promotant^d containing 90 mg of trenbolone acetate and 16 mg of estradiol was administered SC in the caudal aspect of the left ear. During arrival processing, a skin biopsy specimen was collected from each steer and processed. After initial processing, cattle were housed in 20 pens of approximately 100 cattle each and managed in accordance with routine feedlot practices. Cattle were evaluated for signs of illness by trained feedlot personnel. When cattle suspected of being ill were identified, they were moved to a cattle-handling facility and treated according to treatment protocols developed by the consulting veterinarian (DUT). Cattle were typically deemed to be chronically ill if they failed to respond favorably to the administration of 3 courses of treatment. These cattle were removed from group 1 and transferred to a separate feedlot for convalescent cattle. Cattle that died underwent postmortem evaluation, and cause of death was assigned under the supervision of the consulting veterinarian (DUT). If an animal with respiratory tract disease failed to respond favorably to an antimicrobial regimen or after responding favorably developed a subsequent episode of respiratory tract disease, it was treated with a different antimicrobial agent. If an animal required a fourth treatment for respiratory tract disease, it was removed from the study. The first, second, and third treatment regimens were enrofloxacin^e at 12.5 mg/kg (5.7 mg/lb), florfenicol^f at 40 mg/kg (18.2 mg/lb), and oxytetracycline^g at 20 mg/kg (9.1 mg/lb). All antimicrobial drugs were administered SC in the cervical region in accordance with beef quality assurance protocols.

Where possible, skin biopsy specimens were collected from the cattle at the time of treatment for disease or death. Steers were shipped to a commercial abattoir^h when it was deemed that most had attained desirable body weight and composition.

Group 2—Skin biopsy specimens were collected from 1,383 chronically ill cattle as they arrived at a feedlot used to house convalescent cattle. Cattle that arrived at this convalescent feedlot from March through July 2002 were enrolled in the study. These cattle were transferred from 7 feedlots located in southwest Kansas (n = 2) and the Texas Panhandle (5), which included those feedlots from which group 1 and 3 cattle were derived. Under the direction of their consultant veterinarian (DUT), these supplier feedlots deemed cattle to be chronically ill if they required administration of 4 or more treatment regimens for a particular disease or if the disease was deemed refractory to routine treatment protocols.

Group 3—Skin biopsy specimens were collected from cattle during routine postmortem evaluation at a large com-

mercial feedlot located in the northern Texas Panhandle. Specimens were collected from November 2002 through October 2003 and processed as described. Formalin-fixed skin biopsy specimens were stored at the feedlot and submitted in batches throughout the 12-month period.

Sample collection and processing—Commercially available ear notchers were used to excise a 1 × 2-cm biopsy specimen of tissue from the ventral margin of either the left or right ear during postmortem evaluation or while the animal was restrained in a chute. Samples were fixed in neutral-buffered 10% formalin for at least 6 hours prior to further processing. Skin biopsy specimens from group 1 (n = 2,000) were transported to Colorado State University. On arrival, they were transferred from the formalin solution to phosphate-buffered saline solution (PBSS). All other samples were transported to the Texas Veterinary Medical Diagnostic Laboratory in Amarillo, Tex, for analysis.

Formalin-fixed tissue was routinely processed, embedded in paraffin, sectioned at 5 µm, and mounted. Mounted sections were deparaffinized and rehydrated by use of xylenes and a graded series of alcohols. Sections were stained via slight modifications of described methods.¹¹ Those samples processed at Colorado State University were stainedⁱ by use of an automated stainer,^j whereas samples processed at the Texas Veterinary Medical Diagnostic Laboratory were manually stained. Briefly, a solution of monoclonal anti-BVDV antibodies^{k,l} against the conserved 15C5 antigen was applied at a dilution of 1:1,000 for 30 minutes. After 3 rinses in PBSS of 5 seconds each, alkaline phosphatase-labeled secondary antibody^m was applied for 10 minutes. Finally, a fast red chromagen was applied for 10 minutes. After rinsing 3 times for 5 seconds each in deionized water, sections were counterstained with hematoxylin. Positive and negative controls were stained with each batch of skin biopsy specimens. Positive controls included esophageal tissue from an animal that died from mucosal disease and skin from a PI animal. Nonimmune mouse serum was used in place of the primary antibody to generate negative controls. Processed samples were evaluated histologically for specific staining patterns described by Njaa et al¹⁰ as characteristic of a persistent BVDV infection. For the purposes of this study, cattle were classified as PI if typical staining was detected in multiple hair follicles and epithelial cells of the follicular isthmus and infundibulum. If atypical staining was observed, such as limited focal staining, a follow-up skin biopsy specimen was collected where possible and routinely processed as described. If no follow-up specimen was collected, the animal with an atypical staining pattern was classified as not PI.

Statistical analyses—For group 1 cattle, prevalence estimates of cattle PI at arrival, treatment for disease, death, or rejection from the study because of chronic illness were generated. A Wilson approximation for exact confidence intervals (CIs) was used to generate estimates of precision of prevalence.¹² Prevalence and precision were similarly calculated for groups 2 and 3.

A cohort study was performed with group 1 cattle to evaluate a potential spatial association of PI cattle with the risk and incidence of treatment for respiratory tract disease of in-contact cattle. The analysis proceeded at 2 levels on the basis of separate definitions of exposure. In the first analysis, cattle were considered exposed if they were penmates of a PI animal; all other cattle were considered not exposed. The second definition of exposure was broader and included penmates and those cattle in pens adjacent to a pen containing a PI animal. The outcome of interest was cattle with respiratory tract disease that required treatment as determined by trained feedlot animal health personnel. Both risk and incidence were calculated for the exposed and not exposed

cohorts and compared. For risk, the denominator was cattle at risk, whereas for incidence, the denominator was time (head [ie, cattle]-days) at risk. Cattle only contributed time at risk prior to their initial treatment for respiratory tract disease. Once initially treated, they did not contribute to time at risk even if they responded favorably and were returned to their home pen.

Descriptive estimates of morbidity rate (risk and incidence), mortality rate, and other cattle losses (cattle rejected from the study because of chronic illness) were generated for exposed and not exposed cohorts. Relative risk, rate ratios and their 95% CI, and *P* values were calculated via freely¹¹ and commercially¹⁰ available software packages. Within each software package, *P* values were calculated via the χ^2 or Poisson distributions for risk and incidence, respectively. Evaluations of feedlot-to-feedlot and submission-to-submission variation for groups 2 and 3, respectively, were performed with χ^2 goodness of fit tests. Population attributable fraction, an estimate of total disease attributable to exposure, was calculated by use of the estimators of relative risk and rate ratio. For all comparisons, *P* < 0.05 was considered significant.

Results

Group 1—Two thousand cattle with mean \pm SEM arrival weight of 318.1 \pm 0.62 kg (699.8 \pm 1.4 lb) were enrolled into this aspect of the study. These cattle were received and processed in 5 groups during a 9-day period from February 26 to March 6, 2002. The groups of cattle were processed within approximately 24 hours of arrival on February 27 (*n* = 400), March 1 (602), March 4 (400), March 5 (401), and March 6 (197). Steers were housed in 20 pens containing a mean, median, minimum, and maximum of 100, 100, 95, and 107 cattle, respectively. The pens were all located on the west side of a single north-south feed alley. The 20 pens were arranged in 2 groupings of 10 consecutive pens (pen numbers 21 to 30 and 33 to 42). The cattle housed in pens 31 and 32 were nonstudy cattle of unknown BVDV status.

Steers were slaughtered after a mean \pm SE of 161.5 \pm 0.6 days after arrival. All cattle were sent to a commercial abattoir on the same day, in contrast to staggered arrival processing. Of the cattle enrolled in the study, 6.5% (*n* = 130) were treated for disease. The vast majority (98%) of treatment regimens were administered to cattle with signs of respiratory tract disease. Of the cattle treated, 69.5% (*n* = 91) were treated once, whereas 15.3% (20), 10.7% (14), and 4.5% (6) were treated 2, 3, and 4 or more times, respectively. Twelve (0.6%) cattle were rejected from the study because of chronic illness including respiratory tract disease (*n* = 8), enteritis (1), and miscellaneous conditions (3; not including respiratory tract disease, mucosal disease, lameness, or ruminal tympany). Twenty-one (1.05%) cattle died during the course of the study. Attributed cause of death included respiratory tract disease (*n* = 5), BVDV (9; mucosal disease or acute enteritis), ruminal tympany (3), miscellaneous disor-

ders (3), and lameness (1). Overall, 1.65% (*n* = 32) of cattle did not reach a desirable slaughter weight.

Six cattle were identified as PI with BVDV, yielding a prevalence estimate of 0.3% (95% CI, 0.14 to 0.65). All PI cattle were administered more than 1 treatment regimen; on each occasion, the treatment

Table 1—Variables associated with exposure and respiratory tract disease in feedlot cattle that were either exposed or not exposed to an animal persistently infected (PI) with bovine viral diarrhoea virus. Exposure was defined to include cattle in a pen that contained a PI animal and cattle in adjacent pens.

Variable	Cohort		<i>P</i> value
	Exposed	Not exposed	
No. of pens	9	11	ND
Days on study	159.2	163.4	ND
No. of cattle	897	1109	ND
No. of initial treatments	66	57	ND
Morbidity rate (%)	7.36	5.14	ND
Relative risk (95% CI)	1.43 (1.02–2.02)	ND	0.04
Time at risk (head-days)	134,360	171,973	ND
Incidence (per 10,000 head-days)	4.91	3.31	ND
Rate ratio (95% CI)	1.48 (1.04–2.11)	ND	0.03

ND = Not determined. CI = Confidence interval.

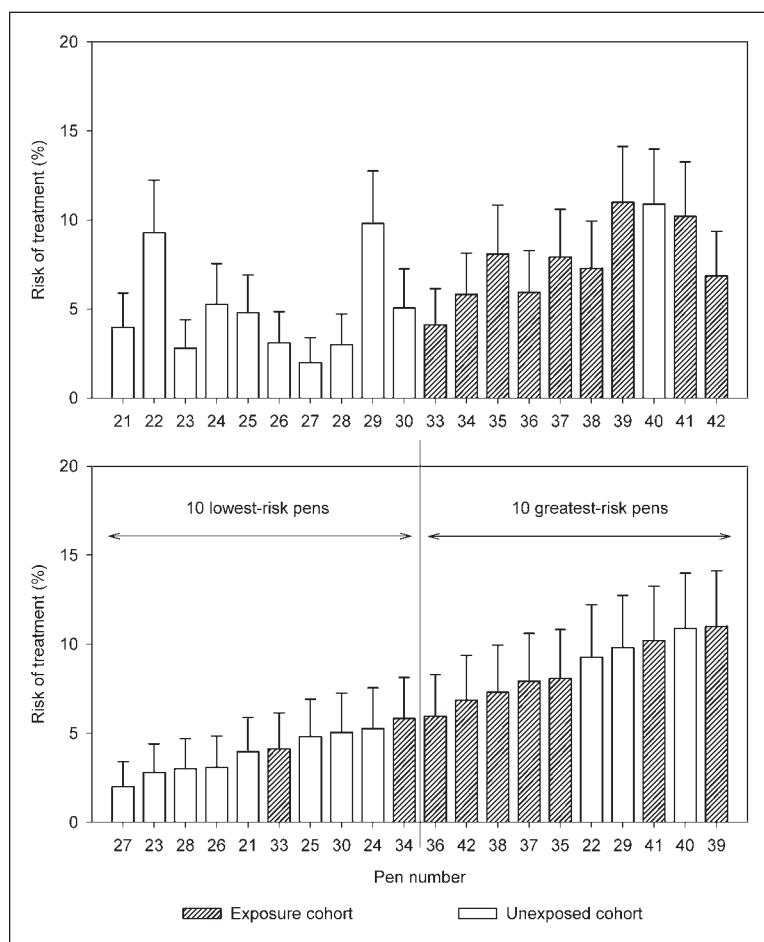


Figure 1—Risk of initial treatment (percentage cattle that received treatment) among the population at risk [mean \pm SE] for respiratory tract disease among feedlot cattle. Cattle persistently infected (PI) with bovine viral diarrhoea virus (BVDV) were located in pens 34 (*n* = 1), 37 (2), 38 (2), and 42 (1). Pens are arranged spatially (top [pens 31 and 32 contained nonstudy cattle of unknown BVDV status]) and in order of increasing risk of initial treatment for respiratory tract disease (bottom).

regimens were administered for respiratory tract disease. Cattle PI with BVDV were administered more ($P < 0.01$) treatment regimens than non-PI cattle that received at least 1 treatment regimen (3.17 vs 1.46 treatments, respectively). All PI cattle were either rejected from the study because of chronic respiratory tract disease ($n = 3$) or died (3). Those PI cattle that died had gross lesions consistent with mucosal disease. Persistently infected cattle deemed chronically ill were rejected 31 ($n = 1$) and 147 (2) days after arrival, whereas the PI animals that died did so 35, 50, and 58 days after arrival. Of the treated, dead, and rejected cattle, 4.6%, 14.3%, and 25%, respectively, were classified as PI with BVDV.

In the first analysis, which evaluated the effect of exposure to a PI animal on morbidity rate, exposure was defined as those cattle within a pen that contained a PI animal. Overall, cattle in 4 pens that contained 402 cattle were considered exposed, whereas cattle in 16 pens that contained 1,598 cattle were considered not exposed. The risk of disease in exposed and not exposed cattle was 7.0% and 5.9%, respectively; these were not significantly different (relative risk, 1.17; 95% CI, 0.74 to 1.69 [$P = 0.60$]). The incidence of disease in the exposed and not exposed cohorts was 4.6 and 3.9 treatments/10,000 head-days, respectively (rate ratio, 1.18; 95% CI, 0.75 to 1.76 [$P = 0.53$]).

In the second analysis, exposure was defined more broadly to include those cattle considered exposed in the first analysis and those cattle in pens adjacent to a pen containing a PI animal (ie, any animal with the opportunity for direct contact with a PI animal). On the basis of this definition, cattle in 9 pens were classified as exposed and cattle in 11 pens were not exposed (Table 1). Cattle exposed to a PI animal had a 43% greater risk ($P = 0.04$) of initial treatment for respiratory tract disease, compared with not exposed cattle (Figure 1). Pens with exposed cattle were more likely to have cattle with greater than mean risk of treatment for respiratory tract disease ($P = 0.03$); cattle in 7 of the 10 pens with cattle with the greatest risk of treatment were exposed to a PI animal, whereas cattle in only 2 of the 10 pens with cattle with the lowest risk for treatment were exposed. Of the initial treatments for respiratory tract disease, 15.9% were attributable to exposure to a PI animal (ie, the population attributable fraction). Cattle treated for respiratory tract disease were typically administered more treatment regimens if they were exposed to a PI animal than if they were not exposed to a PI animal (1.76 vs 1.46 treatments, respectively [$P = 0.04$]).

When incidence rates were compared between cohorts, exposed cattle had 48% greater ($P = 0.03$) incidence of initial respiratory tract disease, compared with not exposed cattle (Table 1). In terms of popu-

lation attributable fraction, 17.4% of the incidence of respiratory tract disease was attributable to exposure to a PI animal. Epidemic and cumulative risk curves were also determined (Figure 2). No adverse effect ($P > 0.3$ for all models) of exposure was detected on risk of death, being rejected from the study, or total cattle loss (death loss plus rejection from the study).

Group 2—Specimens were collected from 1,383 chronically ill cattle. These cattle were derived from 7 feedlots with a mean, minimum, and maximum of 197.4, 35, and 314 cattle sampled per feedlot, respectively. Thirty-six cattle were classified as PI, yielding a prevalence estimate of 2.6% (95% CI, 1.9 to 3.6). There was no evidence that prevalence varied among feedlots (Table 2 [$P = 0.46$]).

Group 3—Specimens were collected from 1,585 cattle at postmortem examination during a 12-month period. Specimens were submitted to the diagnostic laboratory on 12 occasions throughout the year, and there was a mean of 32 days (range, 15 to 75 days) between specimen submissions. Of the cattle from which specimens were collected, 2.5% (95% CI, 1.8 to 3.3; $n = 39$) were classified as PI. Variation in prevalence among batches of specimens was not detected ($P = 0.42$).

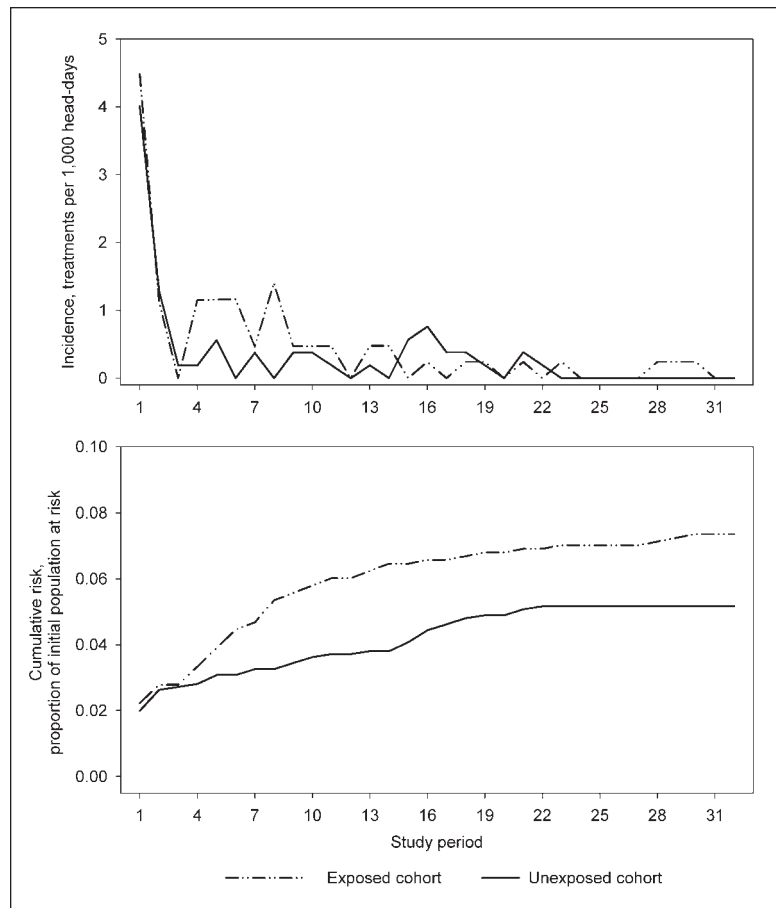


Figure 2—Epidemic curve (top) and cumulative risk (bottom) for cohorts either exposed (dashed line) or not exposed (solid line) to an animal PI with BVDV among feedlot cattle. Exposure was defined to include cattle in a pen that contained a PI animal and cattle in adjacent pens. Each study period represents 5 days. Data for the epidemic curve are number of initial treatments for respiratory tract disease per 1,000 head-days at risk for each study period.

Table 2—Variables associated with PI cattle among 1,383 chronically ill cattle derived from 7 feedlots.

Variable	Feedlot							Overall
	A	B	C	D	E	F	G	
No. of ill cattle	35	42	176	200	293	295	306	1,383
No. of PI cattle	0	3	5	5	10	5	8	36
Prevalence (%)	0	7.1	2.8	2.5	3.4	1.7	2.6	2.6
95% CI	0.0–9.9	2.5–19.0	1.2–6.5	1.1–5.7	1.9–6.2	0.7–3.9	1.3–5.1	1.9–3.6

See Table 1 for remainder of key.

Discussion

Relatively few cattle are PI on arrival at a feedlot. Our prevalence estimate of 0.3% of cattle compared favorably with estimates of others in which 0.15% of 1,995 Mississippi-origin calves^p and 0.23% of 4,705 Iowa feedlot cattle^q were classified as PI with BVDV. In addition, Wittum et al¹³ reported that a similar percentage of ranch calves were PI. Data reported by others^{13–15} indicate that the distribution of PI cattle in the cow-calf setting is extremely clustered. In other words, most ranches do not contain a PI animal; yet when a PI animal is detected, the herd likely contains more than 1. It is possible that PI cattle entering feedlots are similarly clustered by herd of origin. Although it is possible that some or all of the PI cattle identified in group 1 originated from a single herd, it was not possible to evaluate herd-of-origin clustering in our study because the cattle were procured through the auction market systems of various states. If clustering was present in our study, herdmates of the PI cattle would have had longer exposure to the PI cattle than non-herdmates commingled at the auction markets. Further research is required to evaluate herd-level risk when clustering is present.

The PI cattle in our study (group 1) were more likely to require treatment for respiratory tract disease and either become chronically ill or die, compared with cattle that were not PI. This conclusion appears to be supported by the estimates obtained from groups 2 and 3 in which 2.6% and 2.5% of chronically ill and dead cattle, respectively, were determined to be PI with BVDV. Because cattle cannot become PI after birth, these data indicate that PI cattle are overrepresented in the population of chronically ill and dead cattle. In addition, PI cattle typically required administration of more treatment regimens than non-PI cattle that were treated at least once.

It is interesting that exposure to a PI animal appeared to have little effect when exposure was narrowly defined to include just those cattle within the pen of a PI animal. Although not significant, these pens were at a slightly greater risk of disease than not exposed cattle. However, when exposure was defined more broadly to include adjacent pens of a pen containing a PI animal, exposure had a detectable adverse effect on morbidity rate, compared with not exposed cattle. We chose to include adjacent pens in this definition of exposure because frequent cross-fence interactions such as grooming were observed, and water troughs were placed in the fence between pens so that cattle from 2 pens could access the same water trough. In addition, BVDV is known to be highly infectious and it is unreasonable to believe that a cable and post

fence would prevent cross-fence virus transmission. The results of the 2 analyses should not be viewed as contradictory but likely reflect the highly infectious nature of BVDV¹⁶ in that transmission, and therefore BVDV-induced disease, is not necessarily confined within a feedlot pen. In other words, the deleterious health consequences associated with a PI animal extend beyond the fence of a typical feedlot pen. Although our broader definition of exposure was not perfect, it did appear adequate to detect an adverse effect of a spatial association with a PI animal. Incidence of treatment for respiratory tract disease was 43% greater in cattle with the opportunity for direct contact with a PI animal. Moreover, 15.9% of initial treatments for respiratory tract disease were attributable to exposure to an animal PI with BVDV. To our knowledge, this is the first time that the magnitude of excess disease attributable to exposure to a PI animal has been described. Furthermore, those cattle that required treatment for respiratory tract disease typically required more treatments if they were exposed to a PI animal, compared with cattle that were not exposed. This adverse effect on health occurred although all cattle were vaccinated with a vaccine^e containing live types 1 and 2 BVDV. It is tempting to speculate that the excess disease observed in our study was because of transmission of BVDV from PI cattle. This was, however, not examined in our study and requires further epidemiologic research to establish a causal relationship.

Taylor et al¹⁷ followed a pen of 28 PI cattle in a feedlot, and none survived to a desirable slaughter weight. Those cattle presumably provided high-level exposure for each other and may have been at greater risk of death than PI cattle sporadically distributed among cattle not PI with BVDV. In our study, all the PI cattle died or were rejected (because of chronic illness) prior to reaching a desirable slaughter weight; however, all survived for at least 4 weeks or more. This may be of importance because new arrivals are at much greater risk of respiratory tract disease, compared with cattle that have been at the feedlot for greater amounts of time.¹ Ultimately, new arrivals are more susceptible to pathogens than established cattle. Not surprisingly, almost all respiratory tract disease events occur within 4 weeks of arrival.¹ Persistently infected cattle that are present during this period presumably serve as a high-level source of BVDV for in-contact cattle. Interestingly, 33% of group 1 PI cattle survived to within 2 weeks of slaughter. Long-term survival, such as we observed, would facilitate continued high-level exposure to BVDV and may possibly contribute to so-called late-break disease events in which an unexpected epidemic of respiratory tract disease is observed in cattle

that are advanced in the feeding process (eg, > 70 days since arrival).

A weighted prevalence estimate of 0.23% at arrival can be derived by use of our data and those of others.¹⁴ Therefore, among 100,000 cattle arriving at a feedlot, one would expect approximately 230 PI cattle. Given an industry mean² risk of death loss and rejection of 1.42% and 0.7%, respectively, 1,420 and 700 cattle would be expected to die or be sold prior to a desirable slaughter weight. We determined that 2.5% and 2.6% of dead and chronically ill cattle (those typically sold prior to a desirable slaughter weight), respectively, were PI with BVDV. Thus, approximately 176 (ie, 230 minus 54) PI cattle would survive to a desirable slaughter weight and presumably be marketed through routine channels provided our estimates and those of others are accurate. Although this may seem unlikely, others have reported long-term survival of PI cattle.^{8,13,18,q} United States feedlot production practices invariably result in new arrivals being placed in pens adjacent to cattle that have been at the feedlot for considerable time because entire feedlots do not operate on an all-in all-out basis as do some other food production systems. In other words, penloads of cattle are procured and marketed throughout the year primarily on the basis of economic factors. Persistently infected cattle, therefore, have the potential to provide long-term high-level exposure to penmates and adjacent new arrivals even if no PI animal is within a pen of new arrivals.

We did not detect significant feedlot-to-feedlot variation in the prevalence of PI cattle among those deemed to be chronically ill. Although this does not preclude variability in prevalence among feedlots, it does indicate that typically there is little biologically important variation in the prevalence of PI cattle in large feedlots of the southern High Plains.

We also did not detect significant variation in prevalence among batches of specimens submitted during the cross-sectional study of group 3 cattle. Some specimens had the potential to be in formalin for approximately 3 months, whereas the typical time spent in formalin was 48 days. It is generally recommended by most diagnostic laboratories that specimens be processed more expeditiously. Within the Texas Veterinary Medical Diagnostic Laboratory in Amarillo, however, we have observed no detectable signal loss in specimens stored in formalin for several months. Our data suggest that formalin-fixed skin biopsy specimens, when stored appropriately, may be processed several weeks after collection without substantial loss in test sensitivity.

We did not detect an adverse effect on cattle loss (death and rejection from the study). Because the risk of cattle loss was low (1.65%), the number of cattle enrolled in our study resulted in poor statistical power. To detect a similar increase in mortality rate as was observed for morbidity rate (ie, 43%), approximately 10,000 cattle in the exposed and the not exposed cohorts each needed to be enrolled. Further larger-scale epidemiologic research is required to evaluate the spatial association of cattle PI with BVDV and adverse effects on cattle loss and performance.

- a. Dectomax Injectable, Pfizer Animal Health, New York, NY.
- b. Caliber 7, Boehringer Ingelheim Vetmedica, St Joseph, Mo.
- c. Express 5, Boehringer Ingelheim Vetmedica, St Joseph, Mo.
- d. Revalor-IS, Intervet, Millsboro, Del.
- e. Baytril 100, 100 mg/mL, Bayer Animal Health, Pittsburgh, Pa.
- f. Nuflor injectable solution, 300 mg/mL, Schering-Plough Animal Health, Union, NJ.
- g. Bio-Mycin 200, 200 mg/mL, Boehringer Ingelheim Vetmedica, Saint Joseph, Mo.
- h. IBP Inc, Amarillo, Tex.
- i. University of Nebraska Veterinary Diagnostic Laboratory, Lincoln, Neb.
- j. Dako Immunostainer, Model LV 1, Carpinteria, Calif.
- k. Syracuse BioAnalytical, Syracuse, NY.
- l. Bio-Red, Biopath Laboratories, Oklahoma City, Okla.
- m. M-Link-AP, Biopath Laboratories, Oklahoma City, Okla.
- n. EpiInfo 2002, CDC, Atlanta, Ga.
- o. SAS system version 8.02 for Windows, SAS Institute Inc, Cary, NC.
- p. Loneragan GH, Thomson DU, Montgomery DL, et al. Epidemiological investigation of feedlot cattle persistently infected with BVDV (abstr). 83rd Annu Meet Conf Res Workers Anim Dis 2002;32.
- q. O'Connor AM, Sorden SD, Apley MD. The association between persistently bovine viral diarrhea-infected calves and pen levels of morbidity and mortality in an Iowa feedlot (abstr). 36th Annu Conv Am Assoc Bovine Pract 2003;152.

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Selected abstract for JAVMA readers from the American Journal of Veterinary Research

Effects of sulfamethoxazole-trimethoprim on thyroid function in dogs

Linda A. Frank et al

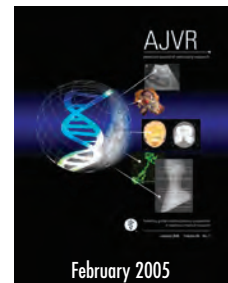
Objective—To evaluate effects of trimethoprim-sulfamethoxazole (T/SMX) on thyroid function in dogs.

Animals—6 healthy euthyroid dogs.

Procedure—Dogs were administered T/SMX (14.1 to 16 mg/kg, PO, q 12 h) for 3 weeks. Blood was collected weekly for 6 weeks for determination of total thyroxine (TT₄), free thyroxine (fT₄), and canine thyroid-stimulating hormone (cTSH) concentrations. Schirmer tear test was performed weekly. Blood was collected for CBC prior to antimicrobial treatment and at 3 and 6 weeks.

Results—5 dogs had serum TT₄ concentrations equal to or less than the lower reference limit, and 4 dogs had serum fT₄ less than the lower reference limit after 3 weeks of T/SMX administration; cTSH concentrations were greater than the upper reference limit in 4 dogs. All dogs had TT₄ and fT₄ concentrations greater than the lower reference limit after T/SMX administration was discontinued for 1 week, and cTSH concentrations were less than reference range after T/SMX administration was discontinued for 2 weeks. Two dogs developed decreased tear production, which returned to normal after discontinuing administration.

Conclusions and Clinical Relevance—Results suggested that administration of T/SMX at a dosage of 14.1 to 16 mg/kg, PO, every 12 hours for 3 weeks caused decreased TT₄ and fT₄ concentrations and increased cTSH concentration, conditions that would be compatible with a diagnosis of hypothyroidism. Therefore, dogs should not have thyroid function evaluated while receiving this dosage of T/SMX for > 2 weeks. These results are in contrast to those of a previous study of trimethoprim-sulfadiazine. (*Am J Vet Res* 2005; 66:256–259)



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RUMINANTS