Descriptive epidemiology of postnatal bovine viral diarrhea virus infection in intensively managed dairy heifers

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Objective—To evaluate risk of bovine viral diarrhea virus (BVDV) infection between birth and 9 months of age for dairy replacement heifers raised under typical dry-lot management conditions.

Design—Longitudinal observational study.

Animals—446 calves.

Procedure—Calves were randomly selected from 2 dairies that used killed and modified-live BVDV vaccines. Repeated serologic and BVDV polymerase chain reaction assays were used to estimate risk of BVDV infection in calves of various ages (1 to 60 days; 61 to 100 days; 101 days to 9 months) and to estimate overall infection rate by 9 months of age.

Results—Risk of BVDV infection increased with age (maximum risk, 150 to 260 days). Proportion of calves infected with BVDV by 9 months of age was higher for dairy A (0.665), compared with dairy B (0.357). Percentage infected with BVDV type I did not differ between dairy A (18.2%) and dairy B (15.2%), whereas percentage infected with BVDV type II for dairy A (50%) was twice that for dairy B (21%). Between 210 and 220 days of age, infection with BVDV regardless of type was >1.3%/d on dairy A and 0.5%/d on dairy B.

Conclusions and Clinical Relevance—Under dry-lot conditions, a considerable amount of BVDV infection may occur before 9 months of age. Risk of infection increases with age. Although dairies may appear to have similar management practices, there can be considerably different risks of BVDV infection among dairies. (J Am Vet Med Assoc 2001;219:1426–1431)

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Bovine viral diarrhea virus (BVDV) has been associated with a variety of clinical and subclinical conditions related to suboptimal productivity, and cattle with subclinical infection have been reported to constitute up to 90% of the cattle in some infected herds. Transmission of BVDV after birth may occur directly by physical contact between susceptible cattle and cattle shedding the virus, by venereal exposure, and by indirect exposure to secretions or excretions containing the virus. Factors influencing efficiency of BVDV transmission within a herd are not known, but they possibly relate to features of management and environment that either favor or impede transmission, including the ratio of susceptible to immune cattle, the proportion of cattle shedding BVDV, cattle density, and virulence or infectivity of the BVDV strains in the herd.

Knowledge of management and environmental factors that affect the risk of cattle being infected with BVDV would improve our ability to control and prevent transmission, thereby minimizing adverse effects of BVDV infection on herd health and productivity. Prerequisite to understanding BVDV transmission in typical herds is information about the potential magnitude of BVDV infection for young replacement cattle during the different management phases, which may be characterized by different levels of passively or actively acquired immunity and by the potential for contact with cattle shedding the virus. Information about when and where cattle become infected will identify periods and management practices associated with high or low transmission risk that would provide insight into which management and host factors may be manipulated to reduce transmission and ultimately infection.

The purpose of the study reported here was to evaluate risk of BVDV infection among young replacement heifers on 2 large dairies with management practices and environments typical of intensively managed dry-lot dairies.

Materials and Methods

Study population—Female calves from 2 central California dairies were enrolled at birth between February 1998 and February 1999 for dairy A and between December 1998 and November 1999 for dairy B. Calves were randomly selected on the basis of the observation of the birth and thatcolostrum had been consumed. Dairies were selected for study, because they had computerized animal records, and their management and vaccination programs typified dry-lot dairies in California. No information was available before the study began on the BVDV statuses of the herds.

Management—Each dairy milked between 1,900 and 2,000 Holstein cows that calved in partially covered corrals accommodating 5 to 10 cows. Two quarts of first-milking colostrum, representing 1 to 10 cows, were fed within the first 1 to 6 hours of birth. Within 24 hours after birth, calves were transported to 1 of 2 calf ranches: calf ranch 1 for calves on dairy A or calf ranch 2 for calves on dairy B. For both calf ranches, calves were housed individually in an elevated wood hutch with plywood roof and slatted floor and walls, which
allowed physical contact with calves in the 2 immediately adjacent hutches. Calves in adjacent hutches were born within 24 hours of each other and may have been from any of the 17 dairies under contract with calf ranch 1, or of the 80 dairies under contract with calf ranch 2. For both calf ranches, calves were fed twice daily 1.9 L of milk collected from cows that were being treated with antimicrobials or were within a milk withdrawal period on local dairies, referred to as “hospital milk.” The milk was heat-treated for 20 minutes at 71.1°C. Colostrum supplements’ were given to calves in the first 24 to 48 hours after birth, and a milk replacer1 was used to supplement hospital milk purchased from surrounding dairies. Calves on calf ranch 1 were weaned at 55 days, and calves on ranch 2 were weaned at 45 days. Approximately 1 week after weaning, calves were moved from the hutches to corrals with an area of 1,065 m² on calf ranch 1 and with an area of 626 m² on calf ranch 2, which each held 85 to 110 calves that represented a mixture of calves from most of the dairies contracted by the ranches. Respective call densities for the corrals at ranches 1 and 2 ranged from 9.7 to 12.5 calves/100 m² and 7.5 to 9.7 calves/100 m², respectively.

At 100 days of age, the calves on calf ranch 1 were returned in groups of approximately 20 calves each to dairy A and placed for 1 to 2 months in a partially covered, vacuum-exposed area of approximately 292 to 1,459 m². Calves were then moved to a larger corral with an area of 1,065 m² on calf ranch 1 and with an area of 1,128 m² on calf ranch 2. At 270 to 300 days of age, heifers on dairy A were moved to a heifer ranch, whereas heifers on dairy B remained on the dairy. For both dairies, calves in the study group were co-mingled throughout the study with calves that represented a mixture of calves from most of the dairies under contract with the ranches. Respective call densities for the corrals at ranch 1 and 2, respectively, were 6.8 calves/100 m² between 100 and 150 days of age; 4.5 calves/100 m² between 150 and 240 days of age; and 3.5 calves/100 m² between 240 and 270 days of age, respectively. Calves were treated for diseases observed in 24 hours of each other and may have been from any of the dairies under contract with the ranches. Respective call densities for the corrals at ranches 1 and 2, respectively, were 9.7 to 12.5 calves/100 m² and 7.5 to 9.7 calves/100 m², respectively. Calves were vaccinated with a killed BVDV vaccine2 at 17 dairies under contract with calf ranch 1, or of the 80 dairies under contract with calf ranch 2. For both dairies, calves in the study group were co-mingled throughout the study with calves that represented a mixture of calves from most of the dairies under contract with the ranches. Respective call densities for the corrals at ranches 1 and 2, respectively, were 6.8 calves/100 m² between 100 and 150 days of age; 4.5 calves/100 m² between 150 and 240 days of age; and 3.5 calves/100 m² between 240 and 270 days of age, respectively. Calves were treated for diseases observed in 24 hours of each other and may have been from any of the dairies under contract with the ranches. Respective call densities for the corrals at ranches 1 and 2, respectively, were 9.7 to 12.5 calves/100 m² and 7.5 to 9.7 calves/100 m², respectively. Calves were treated for diseases observed in 24 hours of each other and may have been from any of the dairies under contract with the ranches. Respective call densities for the corrals at ranches 1 and 2, respectively, were 9.7 to 12.5 calves/100 m² and 7.5 to 9.7 calves/100 m², respectively. Calves were returned to dairy B from ranch 2 at 100 days of age and placed with other calves in corrals ranging in area from 292 to 1,459 m².

At 270 to 300 days of age, heifers on dairy A were moved to a heifer ranch, whereas heifers on dairy B remained on the dairy. For both dairies, calves in the study group were co-mingled throughout the study with calves that represented a mixture of calves from most of the dairies under contract with the ranches. Respective call densities for the corrals at ranches 1 and 2, respectively, were 6.8 calves/100 m² between 100 and 150 days of age; 4.5 calves/100 m² between 150 and 240 days of age; and 3.5 calves/100 m² between 240 and 270 days of age, respectively. Calves were treated for diseases observed in 24 hours of each other and may have been from any of the dairies under contract with the ranches. Respective call densities for the corrals at ranches 1 and 2, respectively, were 9.7 to 12.5 calves/100 m² and 7.5 to 9.7 calves/100 m², respectively. Calves were treated for diseases observed in 24 hours of each other and may have been from any of the dairies under contract with the ranches. Respective call densities for the corrals at ranches 1 and 2, respectively, were 9.7 to 12.5 calves/100 m² and 7.5 to 9.7 calves/100 m², respectively. Calves were treated for diseases observed in 24 hours of each other and may have been from any of the dairies under contract with the ranches. Respective call densities for the corrals at ranches 1 and 2, respectively, were 9.7 to 12.5 calves/100 m² and 7.5 to 9.7 calves/100 m², respectively. Calves were treated for diseases observed in 24 hours of each other and may have been from any of the dairies under contract with the ranches. Respective call densities for the corrals at ranches 1 and 2, respectively, were 9.7 to 12.5 calves/100 m² and 7.5 to 9.7 calves/100 m², respectively. Calves were treated for diseases observed in 24 hours of each other and may have been from any of the dairies under contract with the ranches. Respective call densities for the corrals at ranches 1 and 2, respectively, were 9.7 to 12.5 calves/100 m² and 7.5 to 9.7 calves/100 m², respectively.
proportion that had not seroconverted. Differences in the cumulative proportions of calves that remained uninfected between the 2 dairies were assessed by use of the log rank test. Differences were considered significant at $P < 0.05$.

**Results**

**General infection rates**—Of the 236 calves enrolled from dairy A, 19 (8.0%) died; 9 (3.8%) were lost to follow-up, 1 (0.42%) had repeated positive results of PCR testing for BVDV indicating PI, 1 (0.42%) had a single positive PCR result preceded by several negative test results and was considered to have had a PNI, 43 (18.2%) had serologic evidence of PNI with BVDV type I, 118 (50.0%) had evidence of PNI with BVDV type II, 4 (1.7%) had evidence of PNI with BVDV type I/II, and 51 (21.6%) did not have evidence of PNI with BVDV type I, 126 (60.0%) did have evidence of PNI with BVDV type II, 1 (0.5%) had evidence of PNI with BVDV type I, 44 (21.0%) had evidence of PNI by 270 days of age. Of the 210 calves enrolled from dairy B, 7 (3.3%) died, 2 (1.0%) were lost to follow-up, 1 (0.5%) had evidence of PNI with BVDV type I/II, and 51 (23.3%) did not have evidence of PNI by 270 days of age. Of the 210 calves enrolled from dairy A, 19 (8.0%) died, 9 (3.8%) were lost to follow-up, 1 (0.42%) had repeated positive results of PCR testing for BVDV indicating PI, 1 (0.42%) had a single positive PCR result preceded by several negative test results and was considered to have had a PNI, 43 (18.2%) had serologic evidence of PNI with BVDV type I, 118 (50.0%) had evidence of PNI with BVDV type II, 4 (1.7%) had evidence of PNI with BVDV type I/II, and 51 (21.6%) did not have evidence of PNI with BVDV type I, 126 (60.0%) did not seroconvert to BVDV through 270 days of age.

**Location-specific risk of PNI**—While in the hutches, 2 of the 236 (0.8%) calves from dairy A seroconverted to BVDV type II, and no calves had evidence of PNI with BVDV type I. One of the 210 (0.5%) calves from dairy B seroconverted to BVDV type II, and no calves had evidence of PNI with BVDV type I. After calves were moved from the hutches to corrals at the calf ranch, 3 of the 220 (1.4%) calves that remained at risk from dairy A seroconverted to BVDV type I, and 9 of the 218 (4.1%) at risk seroconverted to BVDV type II. Five of the 203 (2.5%) calves at risk from dairy B seroconverted to BVDV type I, and 5 of 202 (2.5%) calves at risk seroconverted to BVDV type II.

After calves were moved from the calf ranch corrals to corrals at the dairy, and before they reached 9 months of age, 38 of 211 (18.0%) calves at risk from dairy A seroconverted to BVDV type I, 107 of 205 (52.2%) calves at risk seroconverted to BVDV type II, 4 of 218 (1.8%) calves seroconverted to BVDV type I/II, and 52 of 218 (23.4%) calves did not seroconvert to BVDV. Twenty seven of the 197 (13.7%) calves at risk from dairy B seroconverted to BVDV type I, 39 of 197 (19.8%) at risk seroconverted to BVDV type II, and 1 of 203 (0.5%) at risk seroconverted to BVDV type I/II. The risk for BVDV PNI increased as calves were moved from hutch to calf ranch corrals and then to dairy corrals. For dairy A, mean ID for BVDV type-I PNI for calves while in hutch, calf ranch corrals and dairy corrals were 0.0, 0.59, and 1.21 infections/1,000 calf-days at risk, respectively, indicating a slight increase in risk (0.0 to 0.59) after calves were moved from hutch to calf ranch corrals, and a 2.05-fold (1.21/0.59) increase in risk after calves were moved from calf ranch corrals to dairy corrals at the dairy. The highest risk of PNI with BVDV type II (10.89 infections/1,000 calf-days at risk) occurred in the dairy corrals between 210 and 220 days of age. Maximum ID for BVDV exposure in general, which included infection with either type I or type II, was 13.45 at 210 to 220 days of age.

For dairy B, mean ID for BVDV type-I PNI for calves while in hutch, calf ranch corrals, and dairy corrals were 0.0, 0.63, and 0.87 infections/1,000 calf-days at risk, respectively, indicating a slight increase in risk (0.0 to 0.63) as calves were moved from the hutch to the calf ranch corrals and then to dairy corrals, and a slight increase in risk (0.63 to 0.87) after calves were moved from the calf ranch corrals to dairy corrals. The highest risk observed for PNI with BVDV type I was 3.33 infections/1,000 calf-days at risk at 250 to 260 days of age when calves were housed in dairy corrals (Fig 1). Mean ID for BVDV type II were 0.08, 0.50, and 1.31 infections/1,000 calf-days at risk for calves in the hutch, in the calf ranch corrals, and in the dairy corrals, respectively. Risk increased 6.25-fold (0.50/0.08) as calves were moved from hutch to calf ranch corrals and increased 2.6-fold (1.31/0.50) after calves were
moved from the calf ranch back to dairy B. The highest risk of PNI with BVDV type II was 5.23 infections/1,000 calf-days at risk at 210 to 220 days of age in the dairy corrals. Maximum ID for BVDV infection in general, which included infection with either type I or type II, was 5.78 infections/1,000 calf-days at 210 to 220 days of age.

Comparison of BVDV PNI for dairy A and dairy B—As estimated by use of the formula 1 minus cumulative proportion not infected by 270 days, the proportion of calves on dairy A that had been infected with BVDV type I by 270 days (0.182) was not different (P = 0.38) from that of calves on dairy B (0.152). The proportion of calves on dairy A that had been infected with BVDV type II (0.50) was higher (P < 0.001) than that of calves on dairy B (0.21). The proportion of calves on dairy A that had been infected with BVDV type I or type II (0.665) was almost twice as high (P < 0.001) as that for calves on dairy B (0.357).

Mortality—Of the 21 calves that died on dairy A, 2 had previous serologic evidence of PNI with BVDV type I, and 19 had no evidence of previous BVDV infection. On dairy B, none of the 7 calves that died had evidence of BVDV PNI.

Discussion

A major finding of the study reported here was the high rate of BVDV infection in replacement heifers between weaning and 9 months of age. The highest risk for BVDV type I was 9.1 infections/1,000 calf-days at risk on dairy A, indicating that almost 1 in every 100 calves was infected with BVDV type II per day. Considering general BVDV infection without regard to type, infection between 210 and 220 days of age exceeded 1.3%/d (13.45/1,000 calf-days) on dairy A and exceeded 0.5%/d (5.78/1,000 calf-days) on dairy B. By 9 months of age, 66.5% of calves born without evidence of BVDV infection on dairy A and 35.7% on dairy B had evidence of infection with either BVDV type I or type II. These rates of infection are of similar magnitude to those of 40% reported for 7- to 10-month-old Canadian feedlot calves raised under comparable conditions. The similar rates may reflect similarities in management conditions found in feedlots and in dry-lot dairies, including high cattle densities with a large number of cattle per pen or corral that could promote direct animal-to-animal contact with cattle shedding BVDV. The findings of our study indicate that BVDV infection may be highly prevalent in large dairy operations where a high proportion of, if not most, replacement heifers may be exposed to BVDV before their first breeding, even in dairy management systems that use BVDV vaccination programs.

The other important finding is the characterization of when and where the risk of exposure or transmission can be expected to be high for heifer replacement calves raised under the dry-lot type of management. The age and housing-specific risk patterns for PNI observed in our study offer insights into the epidemiology of BVDV transmission for replacement heifers raised under these kinds of intensive management conditions. For calves from both herds, the risk of PNI was low or zero while calves were housed in individual hutches and directly exposed only to the 2 calves in the 2 adjacent hutches. The low risk of PNI during the period calves were in hutches also coincided with the age calves would be expected to have BVDV colostral antibodies. Consequently, it is conceivable that the risk may have been underestimated if colostral antibodies temporarily suppressed or delayed seroconversion or if seroconversion from infection was interpreted instead as being from vaccination. Although control groups were not available in this observational study, the relative segregation and low exposure to BVDV, coupled with the possible presence of high colostral antibody titers, suggest that limited contact between calves and the possible protection afforded by colostral antibodies may have contributed to the low risk of PNI observed during the period calves were housed in hutches.

The movement of calves from the relative isolation of hutches to a potentially extensive exposure to BVDV from the many calves in corrals, together with the diminishing protection from colostral antibodies as calves aged, may have contributed to the observed increase in risk of PNI after calves were moved from hutches into the corrals. Calves in the calf ranch corrals were exposed by direct physical contact to 85 to 110 calves, which would be expected to have increased the likelihood of contact with a PI calf or with a calf shedding BVDV after an acute infection. Additionally, the risk of PNI for genotypes I and II began to increase markedly after calves left the hutches and moved to corrals at the calf ranch and at the dairy, by which time colostral antibodies of some calves would be expected to have decreased to concentrations below that which may confer immunity against BVDV infection. Interestingly, the risk of PNI increased generally after calves were moved to their respective dairies, although the calf density, which could be considered a proxy for the probability of animal-to-animal contact, declined from 7.5 to 12.5 calves/100 m² in the calf ranch corrals to 3.5 to 8.1 calves/100 m² in the corrals at the dairies. A continued increase in the risk of BVDV infection despite declining calf density could suggest that calf density may not have been a factor contributing to transmission or, that by virtue of the intensive nature of the corral housing, the lowest calf density was not sufficiently low to reduce the animal-to-animal transmission of BVDV. Other possible reasons for the increased risk could be that calves were moved to increasingly larger corrals holding more cattle, thereby increasing the probability that they would come in contact with a calf with PI. As the calves aged and moved into increasingly larger corrals, the declining colostral antibodies, with consequent increasing susceptibility, may have been sufficient to offset a decline in calf density, resulting in a net increase in risk of exposure.

It is tempting to speculate that the significantly higher proportion of calves infected with BVDV on dairy A, compared with dairy B, was attributable in some way to differences in management practices and conditions on the 2 dairies, despite the perception that
these 2 dairies were quite similar and typical of intensively managed dry-lot dairies. Some possible explanations for differences could include the following: 1) BVDV vaccination of postpartum cows on dairy B but not on dairy A may have prevented some PI on dairy B; 2) the quality of the vaccination programs, including vaccine handling and administration, may have differed between the 2 calf ranches; 3) although calves on both dairies were potentially exposed at the calf ranches to many BVDV strains from different herds, the 2 dairies may have had different predominant strains or variants that differed in their infectiousness; and 4) the higher rate of PI among the calves on dairy A (0.42%) compared with calves on dairy B (0%), may have contributed to the higher risk of infection on dairy A.

The estimated prevalences and risks of BVDV for the dairies studied here, particularly for BVDV type 1, may have been underestimated if infection occurred close to the time of vaccination and the serologic response was classified as attributable to vaccination rather than infection. It is possible, however, that any such misclassification would have been minimal, because vaccinal titers typically are not sustained > 1:512 for > 3 months, whereas infection titers typically are maintained ≥ 1:512 for > 3 months. Some BVDV type-II infection also would be underestimated if vaccination cross-reactive titers disguised serologic response to infection. However, using the assay and reference viruses as described, the vaccine used here typically induces only a weak BVDV type-II SN titer, if any at all. Vaccine titers for BVDV type I generally were observed to remain ≤ 1:512, whereas infection titers were typically ≥ 1:4,096 and remained elevated.

Although it was not the objective of this study to evaluate BVD vaccination programs, the findings here may offer ideas for development of vaccination strategies. The patterns of BVDV infection risk that developed in the study cattle suggest that vaccination of calves in the first 60 days and again much later at 4 to 9 months of age was not effective in completely preventing infection. Because there were no unvaccinated cattle studied as controls, we were not able to assess whether the vaccination program prevented any infection. We speculate that possible reasons for the high rates of infection among calves that had been vaccinated could include the following: 1) neutralization of vaccine virus by colostral antibodies prevented an effective stimulation of SN antibodies that would subsequently prevent infection; 2) vaccination at ≈ 4 to 9 months of age was too late to prevent infection taking place in calves as young as 3 months of age when they were being exposed to an increasing number of cattle, some of which may have had PI, and when colostral antibody titers would be expected to be low or nil; 3) the high risk of BVDV infection may have been related to use of a vaccine that did not induce sufficient cross-reacting SN antibodies to protect against infection with an antigenically dissimilar BVDV type; and 4) vaccine efficacy has historically been assessed by prevention of clinical disease and not infection. As reviewed recently, there are no published reports that have assessed the efficacy of BVDV vaccination in preventing natural infection, as opposed to clinical disease, under field exposure conditions. Theoretically, however, some efficacy would be expected if the vaccination induced a sufficiently high titer of SN antibodies, which may be expected to neutralize the virus. Possible vaccination strategies suggested by the findings here include the following: 1) vaccinate calves before they leave the relative isolation of hutches, although there may be some neutralization of the vaccine virus by colostral antibodies; 2) administer booster vaccinations through 6 to 7 months of age to promote vaccinal immunity as colostral immunity wanes; 3) repeat boosters as necessary before extensive animal-to-animal contact occurs when calves are moved into pens with high stocking rates; and 4) use vaccines with broad antigenic coverage (type I and type II).

An assessment of BVDV as a cause of calf morbidity and mortality was not possible in our study because of the delay from the time of BVDV infection to detection of a serologic response. If BVDV had caused a calf to become sufficiently sick to be treated, detection of seroconversion would have occurred after the treatment. Consequently, it could not be determined whether or not infection preceded treatment or death. In addition, the largest proportion of treatments occurred while calves were in hutches (1 to 60 days of age) when the risk of BVDV infection was zero or quite low. Moreover, once calves were in the corrals, where surveillance for sick calves was less intense and record keeping was not possible, use of treatment as a proxy for morbidity may have been too crude to detect subtle clinical signs of BVDV infection such as mild fever and short-term inappetence.

Increased transmission of BVDV among replacement heifers as they aged coincided with removal from the relative isolation in hutches, diminished expected protection from colostral antibodies, and increased exposure to a large number of cattle, some of which possibly shed BVDV. Estimates of the risk of infection associated with the various management phases of the heifers quantify the amount of new infections and provide a baseline of risk from which benefits of control programs can be based.

References

2. Calf ranch 1: Nutra-Melk Pre-Starter Concentrate Herd Milk Replacer, Tulare, Calif; Calf ranch 2: 20-20 Gold Label Milk Replacer (nonmedicated), Calva Products Co Inc, Acampo, Calif; and Lawley’s Supplemented Whole Milk Fortifier and Extender, Lawley’s Inc, Modesto, Calif.
3. Elite 4HS, Bio-Ceutic, St Joseph, Mo.
4. Express 4, Bio-Ceutic, St Joseph, Mo.
5. Odyssey-3 L V + Lepto 5, AgriLabs, St Joseph, Mo.
References