Predicted ages of dairy calves when colostrum-derived bovine viral diarrhea virus antibodies would no longer offer protection against disease or interfere with vaccination

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Objective—To develop models that could be used to predict, for dairy calves, the age at which colostrum-derived bovine viral diarrhea virus (BVDV) antibodies would no longer offer protection against infection or interfere with vaccination.

Design—Prospective observational field study.

Animals—466 calves in 2 California dairy herds.

Procedure—Serum BVDV neutralizing antibody titers were measured from birth through 300 days of age. The age by which colostrum-derived BVDV antibodies had decayed sufficiently that calves were considered susceptible to BVDV infection (ie, titer ≤ 1:16) or calves became seronegative was modeled with survival analysis methods. Mixed-effects regression analysis was used to model colostrum-derived BVDV antibody titer for any given age.

Results—Half the calves in both herds became seronegative for BVDV type I by 141 days of age and for BVDV type II by 114 days of age. Rate of antibody decay was significantly associated with antibody titer at 1 to 3 days of age and with whether calves were congenitally infected with BVDV. Three-month-old calves were predicted to have a mean BVDV type-I antibody titer of 1:32 and a mean BVDV type-II antibody titer of 1:16.

Conclusions and Clinical Relevance—Results provide an improved understanding of the decay of BVDV-specific colostrum-derived antibodies in dairy calves raised under typical field conditions. Knowledge of the age when the calf herd becomes susceptible can be useful when designing vaccination programs aimed at minimizing negative effects of colostrum-derived antibodies on vaccine efficacy while maximizing overall calf herd immunity. (J Am Vet Med Assoc 2002;221:678–685)

Bovine viral diarrhea virus (BVDV) infection is widespread in many cattle populations and has been associated with a variety of economically important conditions with high morbidity and mortality rates, including respiratory tract disease and diarrhea. Infection with BVDV can also manifest as subclinical disease with adverse long-term effects, such as diminished fertility and reproductive efficiency. In some herds, as many as 80% of replacement heifers have been found to be exposed to field strains of BVDV before 10 months of age, suggesting that considerable BVDV transmission may take place among vaccinated heifers before their first breeding. Such high rates of infection among cattle on large, well-managed dairies indicate that factors contributing to calf herd immunity, including duration and magnitude of colostrum-derived antibody protection and the potential for interaction with vaccination, need to be more completely understood before control of BVDV infection can be appropriately addressed.

Provision of a high concentration of high-quality antibodies through colostrum is recognized as a key management strategy in reducing susceptibility to infectious agents in general, as well as in promoting overall herd immunity for a group or population of calves. Calf herd immunity to BVDV, defined as the ability of a herd or group of calves to resist BVDV infection or to experience minimal disease resulting from infection, would depend conceptually on the combined individual immunity of all calves in the herd or group and on the likelihood of contact and subsequent disease transmission among calves. The higher the proportion of calves with inadequate or inappropriate immunity, the higher the proportion of susceptible calves and the lower the overall herd immunity. Although many management programs for rearing calves attempt to reduce contact among calves by housing them in individual hutches or in small groups before weaning, it may be too costly or impractical to maintain the same degree of isolation after calves are weaned. Consequently, preventing transmission of infectious diseases, such as BVDV infection, in young calves has relied heavily on provision of passive immunity through appropriate colostrum management. Passive immune protection wanes and calves become increasingly more susceptible to infection as colostrum-derived antibodies decay. Consequently, in addition to providing passive protection through colostrum management programs, most dairies and calf-raising operations vaccinate young calves against BVDV in an attempt to minimize severe disease among calves with failure of passive transfer of BVDV antibodies in colostrum.
For calves that have adequate titers of colostrum-derived BVDV antibodies, it is not known whether vaccination at a young age can negatively impact the duration of passive immune protection or whether vaccine efficacy is affected by the magnitude of the colostrum-derived antibody titer. Evidence that BVDV antibodies from colostrum can interfere with the effectiveness of BVDV vaccination by neutralizing vaccine virus has been the basis for recommendations that vaccination be delayed until colostral antibodies have decayed to low or undetectable concentrations. However, the age at which colostrum-derived BVDV antibody concentrations in calves raised under modern systems of dairy management decay to a point at which they no longer interfere with vaccination is not known. Although colostrum-derived BVDV antibodies have been found to persist for 6 to 10 months in calves, it is not known whether calves used in these studies would be representative of calves from dairies employing vaccination and colostrum management procedures currently typical of large modern dairies.

Knowledge of the age at which calves in a herd can be expected to become susceptible to infection following loss of passive immune protection and the age at which colostrum-derived antibodies would be unlikely to interfere with vaccination is a prerequisite for developing logical strategies to prevent BVDV infection and disease in calves. Because a variety of factors may influence the rate of antibody decay, however, a realistic understanding of the decay of colostrum-derived BVDV antibodies among dairy calves raised under typical management practices and field conditions is required. In general, the present study was designed to characterize the decay in colostrum-derived BVDV neutralizing antibodies among dairy calves raised under typical dry-lot management conditions, with a focus on herd immunity, as opposed to immunity in individual calves. Specifically, the purpose of the study reported here was to develop models that could be used to predict, on a herd basis, the age at which colostrum-derived BVDV antibodies would no longer offer protection against BVDV infection or associated disease in calves and would no longer interfere with BVDV vaccination.

Materials and Methods

Animals—Calves were enrolled between July 1998 and November 1999 on 2 commercial California dairies typical of intensively managed dry-lot dairies in the Central Valley of California. Additional calves from 1 of these dairies that were subjects of a BVDV vaccine trial, reported elsewhere, were included in the study to assess the effect of BVDV vaccination on decay of colostrum-derived BVDV antibodies. Calves in the vaccine trial were enrolled between July and September 1999. A previous study involving these 2 dairies documented the extent of BVDV transmission in heifers up to 9 months of age without apparent clinical signs of BVDV-associated disease.

Pertinent management practices of the dairies included in the present study have been described elsewhere (designations of the herds as A and B in the present study match designations in the previous study). Briefly, the herds were selected for study because they were believed to represent typical large, intensively managed dry-lot dairies milking between 1,900 and 2,000 Holstein cows. For both herds, a modified-live BVDV vaccine was administered 1 to 2 months before heifers were bred for the first time. In herd A, a modified-live BVDV vaccine was also administered 20 to 30 days after parturition. Within 1 to 6 hours after birth, calves were given 1.9 L of pooled, first-milking colostrum from multiparous cows. Within 24 hours after birth, calves were transferred to calf ranches under contract to raise heifer calves for each dairy, where they were housed in individual hutches during the first 50 to 60 days after birth and subsequently moved to corrals. Calves were returned to their respective dairies at 100 days of age. For calves from herd A, a killed BVDV vaccine was given at 16 and 47 days of age, and a modified-live BVDV vaccine was given at 80 and 240 days of age. For calves from herd B, a killed BVDV vaccine was given at 15 days of age, and a modified-live BVDV vaccine was given at 45 and 180 days of age. Vaccinated calves in the vaccine trial were given a killed BVDV vaccine at 15 days of age, a modified-live BVDV vaccine and leptospira bacterin at 45 days of age, and a modified-live BVDV vaccine at 180 days of age. Control calves in the vaccination trial were given a leptospira bacterin and modified-live virus vaccine without BVDV at 45 days and a modified-live BVDV vaccine at 180 days of age.

Study design and sample collection—The present study was designed as a prospective repeated-measures observational study that would allow us to predict the age by which colostrum-derived BVDV antibody titers would reach specified endpoints. Blood samples were collected from all calves between 1 and 3 days after birth to obtain an estimate of the peak colostrum-derived BVDV antibody titer. Additional samples were collected at 2-week intervals during the first 60 days after birth and at 45-day intervals thereafter through 300 days of age.

For all calves in herd A and calves in herd B that were not involved in the vaccination study, blood samples were also collected prior to administration of colostrum. These samples were tested for BVDV virus with a polymerase chain reaction (PCR) assay to detect congenital BVDV infection. Calves for which results of the PCR assay were positive were retested 30 days later and were considered to be persistently infected with BVDV if results of the second test were also positive. Calves classified as persistently infected were retested several times during the next 6 months to confirm their status. A calf was considered to be congenitally infected with BVDV if BVDV titer of a serum sample obtained prior to administration of colostrum was ≥ 1:4 or if the PCR assay yielded a positive result for the sample collected prior to colostrum administration and negative results for subsequent samples.

Sero logic testing—Serum neutralization (SN) assays incorporating the NA DL and c125 BVDV reference strains were used to determine antibody titers to BVDV types I and II. The SN assay was performed on serial 2-fold dilutions of heat-inactivated serum, with 100 to 500 TCID50, bovine fetal testicle cells, and incubation for 96 hours at 37 C in 5% CO2. Results were reported as the endpoint serum dilution that did not have any detectable cytopathic effects. For samples obtained prior to administration of colostrum, serial 2-fold dilutions ranging from 1:4 to 1:4,096 were tested. For subsequent samples, serial 2-fold dilutions ranging from 1:8 to 1:4,096 were tested, and calves were considered to be seronegative if results of the SN assay for the 1:8 dilution were negative.

To characterize the decay of antibodies derived solely from colostrum without interference by antibodies produced actively as a result of exposure to the virus or vaccination, titers were not considered after detection of field exposure to
BVDV or after titers increased following vaccination at 180 to 240 days of age. Field exposure to BVDV was identified as an increase in titer by 3 dilutions relative to the preceding titer that was unrelated to vaccination.  

Titers included in the analyses were those obtained up to the time the calf died, was sold, became infected following field exposure to the virus, responded to vaccination, or reached 300 days of age, whichever was first.

Statistical analyses—Two different analytic approaches were used to accomplish the objectives of the study. The first approach used survival methods to predict the rate at which titers of colostrum-derived antibodies decayed to ≤ 1:16 or the calf became seronegative. The second approach used nonlinear regression to estimate titer of colostrum-derived antibodies for a specified age. The age at which titer of colostrum-derived BVDV antibodies decayed to ≤ 1:16 was considered important because it has been suggested that calves with SN antibody titers ≤ 1:16 are susceptible to clinical disease secondary to BVDV infection.  

For each calf, the age at which the titer of colostrum-derived BVDV antibodies was ≤ 1:16 and the age at which the calf became seronegative were estimated as the midpoint between age at the time these assay results were first observed and age at the time of the preceding testing. Accelerated failure time survival methods were then used to model the ages at which titer decayed to ≤ 1:16 or the calf became seronegative for BVDV type-I and type-II SN antibody titers. The model used was ln(T) = Xβ + αH + eW, where T represented failure time (ie, age at which titer decayed to ≤ 1:16 or the calf became seronegative), X was the vector of variables in the model, β was the vector of regression coefficients representing the effect of each variable X on the failure time, α was a dispersion parameter, and W was a random error assumed to follow the distribution of choice for the baseline hazard.  

Because, for practical applications, information on individual calf factors (eg, whether calves were congenitally infected with BVDV, peak colostrum-derived BVDV antibody titer, and calf size) is not typically available, survival models were first used to model age at which titer decayed to ≤ 1:16 and age at which calves became seronegative without adjusting for other variables. Ages predicted by this unadjusted model would represent the end of passive protection for a specified age. The age at which titer of colostrum-derived BVDV antibodies decayed to ≤ 1:16 was considered important because it has been suggested that calves with SN antibody titers ≤ 1:16 are susceptible to clinical disease secondary to BVDV infection.  

Additionally, adjusted estimates of median ages at which titer decayed to ≤ 1:16 and calves became seronegative for calves with a particular set of covariates were obtained by including in the model the variables herd (herd A vs B), the natural log of the antibody titer at 1 to 3 days of age (peak colostrum-derived antibody titer), whether the calf was congenitally infected (yes vs no), and calf size (heart girth circumference in centimeters). Ages predicted by this adjusted model would represent the end of passive protection for calves with a specific set of characteristics. Peak colostrum-derived antibody titer was included to adjust for differences in the amount of colostrum absorbed by individual calves, because decay of colostrum-derived antibodies would be expected to be longer for calves with higher peak titers than for calves with lower peak titers.  

The error distribution of the model was selected from a variety of distributions, including the Weibull, log-logistic, log-normal, and logistic distributions. The distribution of choice was determined on the basis of graphical comparisons of plots of the appropriately transformed Kaplan-Meier survival function estimates and comparisons of plots of Cox-Snell residuals for the different distributions.  

A nonlinear mixed-effects regression model was used to estimate age-specific colostrum-derived SN titers to BVDV type I and II from birth through 240 days of age in calves with no evidence of congenital BVDV infection or postnatal exposure to BVDV. Calves for which titers indicated a departure from natural decay, defined as an increase in titer by 2 or more dilutions or an absence of decay, were excluded from this analysis. The model allowed for exponential decay of colostrum-derived antibody titers with the following equation:

\[ y_i = (\beta + b_i + a \cdot \text{HERD}) \cdot e^{-\alpha \cdot \text{AGE}_{ij}} + \epsilon_i \]

where \( y_i \) represented the natural logarithm of the titer for the ith calf at age j. Fixed effect coefficients were represented by \( b_i \), \( a \), \( \alpha \), and \( \gamma \), where \( b_i \) represented the colostral titer at age 0, \( a \) represented the effect of herd on peak titers, \( \alpha \) represented the rate of decay of BVDV antibody titer \( \ln(\text{titer}/d) \), and \( \gamma \) represented the effect of herd on the decay of titers. Random effect coefficients were represented by \( b_i \) and \( d_i \), where \( b_i \) represented the unique effect of peak titer, and \( d_i \) represented the unique effect of antibody decay for each calf on the rate of decay for the calf. The model allowed for different peak titers and rates of antibody decay for each calf and for an assessment of the effect of herd on peak titer and rate of antibody decay. Parametric bootstrap methods were used to obtain 95% confidence intervals for the fitted regression line and 95% prediction intervals for colostrum-derived BVDV antibody titers for calves over a range of ages. Computations were performed with commercial statistical software.

Results

Descriptive statistics—Overall, 466 calves were enrolled in the study, including 150 calves from herd A, 208 calves from herd B, and an additional 108 calves from herd B enrolled in the vaccination trial (52 vaccinated against BVDV and 56 not vaccinated against BVDV). Peak colostrum-derived BVDV antibody titers (ie, titers 1 to 3 days after birth) were available for 451 calves; mean age at the time of sample collection was 1.9 days. Calves in herd A had significantly higher mean peak titers for BVDV type I (antilog of mean \( \ln(\text{BVDV type-I titer}) = 1.665 \)) and for BVDV type II (1.299) than did calves in herd B (mean BVDV type-I titer = 1.545 and mean BVDV type-II titer = 1.221; \( P = 0.037 \) and \( P = 0.078 \), respectively). For calves in the vaccination trial, mean peak titers for colostrum-derived BVDV type-I antibodies were not significantly different (\( P = 0.463 \)) between calves assigned to BVDV vaccination (1.812) and control calves (1.545). Similarly, mean peak titers for colostrum-derived BVDV type-II antibodies were not significantly different (\( P = 0.147 \)) between calves assigned to BVDV vaccination (1.299) and control calves (1.200). Most of the 451 calves tested at 1 to 3 days of age had moderate (1:32 to 1:512) to high (≥ 1:1,024) BVDV antibody titers. Only 3.8 and 7.8% of calves had titers ≤ 1:16 for BVDV types I and II, respectively.
Sixteen of the 150 (10.7%) calves in herd A were congenitally infected with BVDV (12 had a BVDV titer ≥ 1:4 prior to administration of colostrum, 3 had positive PCR assay results prior to administration of colostrum, and 1 had both). Similarly, 16 of the 208 (6.3%) calves in herd B were congenitally infected (13 had a BVDV titer ≥ 1:4 prior to administration of colostrum and 3 had positive PCR assay results prior to administration of colostrum). Calves congenitally infected with BVDV had a significantly (P = 0.079) higher mean peak colostrum-derived BVDV type-II antibody titer (1:369) than did calves that were not congenitally infected (1:240). The proportion of calves without evidence of colostrum-derived antibody decay was significantly (P < 0.001) higher for congenitally infected calves (7/32; 22%) than for calves that were not congenitally infected (3/315; 0.9%). One calf in herd A was identified as persistently infected.

When ages at which titer decayed to ≤ 1:16 and calves became seronegative were repeated, including in the model variables for herd, the natural log of the peak colostrum-derived antibody titer, whether calves were congenitally infected, and calf size, an increase in peak colostrum-derived antibody titer was significantly (P < 0.001) associated with an increase in age for titer to decay to ≤ 1:16 and age for calves to become seronegative for both BVDV types I and II (Table 1). For example, for calves from herd B that were not congenitally infected and had a peak titer of 1:512, median age at which calves became seronegative for BVDV type I was 131 days and median age at which titer decayed to ≤ 1:16 was 100 days (Table 2). In contrast, for calves with a peak titer of 1:32, median ages were 74 and 48 days, respectively. Ages for

### Table 1—Results of accelerated failure-time analysis to predict age at which titers of colostrum-derived bovine viral diarrhea virus (BVDV) antibodies in calves on 2 California dairies decayed to ≤ 1:16 and age at which calves became seronegative

<table>
<thead>
<tr>
<th>Variable</th>
<th>BVDV type-I titer</th>
<th>BVDV type-II titer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Seronegative</td>
<td>Titer ≤ 1:16</td>
</tr>
<tr>
<td></td>
<td>Regression</td>
<td>P value</td>
</tr>
<tr>
<td>Unadjusted model</td>
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<td></td>
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<tr>
<td>Intercept</td>
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</tr>
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<td>Herd A</td>
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<tr>
<td>Adjusted model</td>
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<td></td>
</tr>
<tr>
<td>Intercept</td>
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<td>0.780</td>
</tr>
<tr>
<td>Herd A</td>
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<td>0.304</td>
</tr>
<tr>
<td>Peak titer</td>
<td>20.48</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Congenital infection</td>
<td>38.70</td>
<td>0.003</td>
</tr>
<tr>
<td>Effect of vaccination</td>
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<td></td>
</tr>
<tr>
<td>Intercept</td>
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</tr>
<tr>
<td>Vaccination</td>
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<td>0.070</td>
</tr>
<tr>
<td>Peak titer</td>
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<td>&lt; 0.001</td>
</tr>
<tr>
<td>Interaction</td>
<td>−25.73</td>
<td>0.093</td>
</tr>
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</table>

*Unadjusted model containing a variable for herd but no other covariates. **Herd B was used as the baseline for comparison. Additional model containing variables for herd, peak titer, and congenital infection. Natural log of titer 1 to 3 days after birth. *Congenital infection with BVDV; no congenital infection was used as the baseline for comparison. Adjusted model of the effect of vaccination including a variable for peak titer. *Unvaccinated group was used as the baseline for comparison. Interaction between vaccination and peak titer. NA = Not applicable; interaction term was not included.
Ruminants

table was significantly (colosotum-derived BVDV type-I antibody was unde-
enrolled in the vaccination trial, the age at which colostrum-derived antibody decay among calves
body decay
—In unadjusted analyses of ages for calves that were not congenitally infected (Table 2). 
became seronegative for BVDV type I was 192 days for 
peak titer of 1:2,048, median age at which calves
infected. For example, for calves from herd A with a
between calves that were or were not congenitally
P
≤
1:16 for BVDV type I (P = 0.005) and II (P = 0.032) and age at which
titer decayed to ≤ 1:16 for BVDV type I (P = 0.005) were significantly higher for congenitally infected calves than for calves that were not congenitally infected, but age at which titer decayed to ≤ 1:16 for BVDV type II was not significantly (P = 0.207) different between calves that were or were not congenitally infected. For example, for calves from herd A with a peak titer of 1:2,048, median age at which calves became seronegative for BVDV type I was 192 days for congenitally infected calves and 154 days for calves that were not congenitally infected (Table 2).

Effect of vaccination on predicted ages of antibody decay—In unadjusted analyses of ages for colostrum-derived antibody decay among calves enrolled in the vaccination trial, the age at which colostrum-derived BVDV type-I antibody was undetectable was significantly (P = 0.05) greater for vaccinated than for unvaccinated calves. After inclusion of other factors in the model, evidence was found for an effect of the interaction between vaccination and the natural log of the peak colostrum-derived antibody on age at which colostrum-derived antibody became undetectable for BVDV types I (P = 0.093) and II (P = 0.049; Table 1). This interaction indicated that for calves with an intermediate (1:64 to 1:512) peak colostrum-derived BVDV type-I antibody titer or a low (≤ 1:32) peak colostrum-derived BVDV type-II antibody titer, ages at which colostrum-derived BVDV type-I and -II antibodies became undetectable were greater for BVDV-vaccinated calves than for unvaccinated calves. For calves with high (> 1:512) peak colostrum-derived BVDV type-I antibody titers or moderate to high (> 1:32) peak colostrum-derived BVDV type-II antibody titers, however, ages at which colostrum-derived antibodies became undetectable were greater for unvaccinated calves than for vaccinat-
calves. For example, for calves with a peak colostrum-derived BVDV type-I antibody titer of 1:32, median age at which colostrum-derived antibodies became undetectable was 182 days for vaccinated calves and 78 days for unvaccinated calves. In contrast,
for calves with a peak colostrum-derived BVDV type-I antibody titer of 1:2,048, median age at which colostrum-derived antibodies became undetectable was 178 days for vaccinated calves and 182 days for unvaccinated calves. For calves with a peak colostrum-derived BVDV type-II antibody titer of 1:32, median age at which colostrum-derived antibodies became undetectable was 85 days for vaccinated calves and 73 days for unvaccinated calves. In contrast, for calves with a peak colostrum-derived BVDV type-II antibody titer of 1:2,048, median age at which colostrum-derived antibodies became undetectable was 116 days for vaccinated calves and 160 days for unvaccinated calves.

Estimation of colostrum-derived BVDV antibody titers—Data from 227 calves, 99 from herd A and 128 from herd B, were used to estimate BVDV type-I antibody titers, and data from 285 calves, 123 from herd A and 162 from herd B, were used to estimate BVDV type-II antibody titers (Table 4). Estimates of BVDV type-I antibody titers were calculated separately for herds A and B because adding a variable for herd improved the fit of the model (likelihood ratio test; P = 0.06), indicating that titers were different for the 2 herds. Inclusion of a variable for herd, however, did not significantly improve the fit of the model for BVDV type-II antibody titers (likelihood ratio test; P = 0.36). Therefore, estimates of BVDV type-II antibody titers were calculated for the 2 herds combined. Estimated mean rates of decay (ln[titer]/d) for BVDV type-I antibody titers were 0.0077 for herd A and 0.0082 for herd B. Estimated mean rate of decay for BVDV type-II antibody titers was 0.0082 for both herds. Estimated mean BVDV type-I and -II titers and 95% bootstrap prediction intervals were calculated as a function of age (Fig 2 and 3). This analysis indicated that predicted age at which calves would be seronegative for BVDV type I was 210 days for both herds A and B and predicted ages at which mean titer would be approximately 1:16 was between 120 and 150 days for calves in herd A and between 90 and 120 days for calves in herd B. Predicted age at which calves would be seronegative for BVDV type II was 180 days, and predicted age at which mean titer would be approximately 1:16 was between 90 and 120 days.

Discussion

Results of the present study provide 2 alternative means of assessing the degree of colostrum-derived protection against BVDV infection for dairy calf populations of various ages. The estimates calculated in the present study can potentially be used to help direct the timing of BVDV vaccination so as to minimize neutralization of vaccinal virus by
colostrum-derived antibodies and maximize herd immunity.

One approach used in the present study allowed prediction of the ages by which specified percentages of the calf herd could be expected to be susceptible to BVDV infection, as indicated by having no detectable colostrum-derived BVDV antibodies or by having a colostrum-derived antibody titer $\leq 1:16$. These predicted ages potentially have application in the development of management strategies to control and prevent BVDV infection. For example, if owners of the 2 herds in this study wanted to adopt a strategy to begin vaccinating calves with a modified-live BVDV type-I vaccine when 50% of the calves had type-I titers $\leq 1:16$, then the owner of herd A should begin vaccinating calves at approximately 111 days of age and the owner of herd B should begin vaccinating calves at approximately 107 days of age.

The other approach used in the present study offered a means for estimating age-specific colostrum-derived BVDV antibody titers. These estimates can be used for herds with management similar to the herds in this study to identify whether colostrum-derived antibody titer at a specified age would be high enough to offer the necessary level of protection. For example, if one were to consider a BVDV type-II titer of 1:32 to be the minimal titer necessary for protection against disease, the calf herd could be expected to become susceptible after 70 days of age, which is the age when the upper 95% confidence limit of the mean titer for all calves reaches 1:32. If individual calves were of interest, rather than the herd as a whole, then the 95% prediction limits would indicate that individual calves could be expected to become susceptible when they were between about 30 and 120 days old.

Earlier estimates of how long colostrum-derived BVDV antibodies could be expected to persist ranged from 6 to 10 months. These estimates have been used in developing recommendations for BVDV vaccination programs. However, these estimates generally were longer than the estimated ages in the present study at which calves became seronegative for BVDV types I (141 days) and II (114 days). Although the reasons for the variation in these estimates are not known, differences may well have been attributable to differences in sample sizes, analytic methods, serologic tests used, and protocols for colostrum administration, which in previous studies may not have been typical of those found on commercial dairies such as the ones used in the present study. A recent study that used a slightly larger number of calves than earlier studies and that was conducted under conditions more similar to field conditions reported estimates comparable to, but shorter than, estimates in the present study. The mean ages by which calves were predicted to become seronegative in that study were 118 days for BVDV type I and 94 days for BVDV type II. A possible factor that may have resulted in the slightly shorter longevity of colostrum-derived antibodies in that study was the absence of calves congenitally infected with BVDV, which as found in the present study, maintain BVDV antibodies for a longer time.

Several factors were found to influence colostrum-derived BVDV antibody titers among calves in the present study. Congenital BVDV infection was associated with a decreased proportion of calves that were seronegative or had a titer $\leq 1:16$ at any given age. The higher peak colostrum-derived antibody titers (ie, titers at 1 to 3 days of age) and the longer duration of antibody persistence for calves congenitally infected with BVDV, compared with calves that were not congenitally infected, likely were a result of BVDV exposure in utero that stimulated active antibody production that continued after birth. Even though the presence of congenitally infected calves may increase the duration of antibody protection for a calf herd, little is known about the immunology of congenital BVDV infection, how congenital infection affects the overall immune system, or the potential for long-term effects of congenital infection.

Vaccination for BVDV by 45 days of age was associated with prolonged persistence of BVDV antibodies, conditional on peak colostrum-derived BVDV antibody titer. The nature of the interaction between vaccination and peak titer indicated that vaccination was effective in promoting BVDV antibody production if the calf had a moderate or low peak colostrum-derived BVDV antibody titer, as would be the case if the calf was deprived of colostrum or had consumed colostrum with a minimal concentration of BVDV antibodies. However, vaccination was not effective in changing the duration of antibody persistence if the calf had consumed a large amount of BVDV antibody in the colostrum. For example, median ages by which calves with a peak BVDV type-I titer of 1:32 would be seronegative for BVDV type I were 182 days for vaccinated calves and 78 days for unvaccinated calves. For calves with a peak titer of 1:2,048, however, median ages by which calves would be seronegative were about the same for vaccinated (178 days) and unvaccinated (182) calves. Consequently, one would expect early calfhood BVDV vaccination to augment BVDV antibody titers in calves with lower levels of passive immunity, but such early vaccination may not be cost-efficient for calves with good passive immunity.

Estimates from the present study for mean BVDV antibody titers for a given age and predicted ages when a specified proportion of calves would become susceptible to infection have practical applications for practitioners assessing BVDV immune status of populations of dairy calves. Several factors were found to affect the rate of decay of colostrum-derived BVDV antibodies, including peak titer, whether calves were congenitally infected, the interaction between peak titer and vaccination, and various undefined differences between herds. Ideally, such factors should be taken into account when attempting to plan an appropriate vaccination program. However, because in most situations testing to identify congenitally infected calves and peak titers is not feasible, we analyzed our data by ignoring the effects of congenital infection and peak titer. The resulting curves, representing predicted ages for antibody decay and estimated titers at various ages, can be regarded as generic models for decay of colostrum-derived BVDV antibodies in dairy calves from herds with similar management conditions as those in the present study. Of course, one should expect deviation from the model, depending on how much the prevalence of congenital infection, the vaccination scheme, and peak antibody titers for the herd of interest vary from those for herds in the present study. If management conditions in a specific herd are not comparable with condi-
tions for herds in this study and quality of passive trans-
fer in the herd is not known, an alternative approach
would be to collect blood samples from calves at 1 to 3
days of age and test for peak colostrum-derived BVDV
antibody titer. If the estimated peak titer is lower or high-
er that the peak titer for the herds in the present study
(approx 1:512 for BVDV type I and 1:256 for BVDV type
II), the age by which 50% of the call herd would be
expected to be susceptible to infection should be adjust-
ed up or down. Although not directly applicable, because
estimates of the rate of antibody decay are specific for
peak titer and prevalence of congenital infection, esti-

mated median ages at which calves in the present study
became seronegative or had titers ≤ 1:16 could be used as
references to decide on appropriate vaccination times.
For example, if estimated peak colostrum-derived BVDV
type-I antibody titer in a specific herd was 1:2,048, vac-
cination could be delayed until approximately 160 days;
but if the estimated average peak titer was 1:32, vaccina-
cation could be started as early as about 70 days of age.

In summary, estimates provided here offer an
improved understanding of the decay of colostrum-
derived BVDV antibodies in calves and of the period of
passive protection for dairy calves raised under typical
intensively managed systems. The data have clinical
application in BVDV control programs, as they can be
used to estimate the age by which a group of calves
would be expected to lose passive protection. Such
information could possibly be used to develop vaccina-
tion and c alf management programs aimed at minimiz-
ing the risk of BVDV infection and associated disease.

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