# Association between infection of the respiratory tract attributable to bovine coronavirus and health and growth performance of cattle in feedlots

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**Objective**—To determine the association between respiratory tract infection with bovine coronavirus (BCV), treatment for respiratory tract disease, pulmonary lesions at slaughter, and average daily gain in cattle in feedlots.

**Animals**—837 calves in feedlots in Ohio and Texas.

**Procedure**—Nasal swab specimens were obtained from cattle at arrival in a feedlot (day 0) and at various times during the initial 28 days after arrival. Specimens were tested for BCV, using an antigen-capture ELISA. Serum samples were obtained at arrival and again 28 days after arrival and tested for antibodies to BCV, using an antibody-detection ELISA. Information was collected regarding treatment for cattle with respiratory tract disease and average daily gain during the feeding period. Pulmonary lesions were evaluated at slaughter.

**Results**—Cattle shedding BCV from the nasal cavity and developing an antibody response against BCV were 1.6 times more likely to require treatment for respiratory tract disease than cattle that did not shed the virus or develop an immune response against BCV. Additionally, cattle that shed BCV from the nasal cavity were 2.2 times more likely to have pulmonary lesions at slaughter than cattle that did not shed the virus. The BCV shedding or seroconversion status did not affect average daily gain.

**Conclusions and Clinical Relevance**—Bovine coronavirus infects feedlot cattle and is associated with an increased risk for cattle developing respiratory tract disease and pulmonary lesions. Development of appropriate control measures could help reduce the incidence of respiratory tract disease. (*Am J Vet Res* 2000;61:1062–1066)

**B**ovine coronavirus (BCV) was first recognized as a cause of potentially fatal diarrhea of neonatal calves in 1972.[1] Additional investigations found this large, enveloped, single-stranded RNA virus in outbreaks of calf diarrhea[2-4] and winter dysentery of adult dairy cattle[5,6] as well as in calves with pneumonia.[4,7-9] In 1996,

investigators[10] isolated BCV from 38 of 100 cattle involved in outbreaks of respiratory tract disease at feedlots in Kansas and Arizona. That finding has prompted concern about the possible role BCV may play in the **bovine respiratory disease complex (BRDC)** of feedlot cattle.

Considering the roles of multiple viruses in BRDC, it seems likely that BCV, with its tropism for the respiratory tract and association with pneumonia in calves, also could contribute to the pathogenesis of BRDC. Although evidence of BCV infections in feedlot cattle is available, it is still unclear the role it may play in BRDC, because we found that the virus also could be isolated from apparently healthy cattle.[a] To better define the role of BCV in BRDC, we surveyed 837 mixed-breed cattle entering 4 feedlots to describe shedding patterns of BCV from the respiratory tract and rates of exposure. Information was collected on treatment rates for cattle with respiratory tract disease, pulmonary lesions at slaughter, and average daily gain to enable us to identify associations of BCV shedding and seroconversion with these outcomes.

## Materials and Methods

**Study population**—From spring 1996 through fall 1997, 837 cattle (9 groups) that were entering 4 feedlots were surveyed for BCV in the nasal cavity. All cattle were between 4 and 7 months old and were predominantly mixed-breed calves. Samples were collected from clinically normal cattle and those with signs of respiratory tract disease. Cattle at 3 feedlots in Ohio (Jackson, Lucasville, Wooster) and 1 in Texas (Amarillo) were used, as described elsewhere.[11] All cattle were vaccinated at arrival at their respective feedlots, using multivalent vaccines against agents including **bovine herpesvirus-1 (BHV-1)**, **bovine viral diarrhea virus (BVDV)**, **bovine respiratory syncytial virus (BRSV)**, and **parainfluenza-3 (PI-3)** virus. Information was collected on treatment for cattle with respiratory tract disease and average daily gain. Cattle were treated in accordance with criteria established for each feedlot regarding identification of sick cattle and treatment protocol. Although the definition of cattle with respiratory tract disease varied slightly between feedlots, it general-

ly consisted of an increase in rectal temperature (> 39.4 C), weight loss or failure to gain weight, inappetence, signs of depression, coughing, nasal discharge, or any combination of these. Affected cattle were identified by experienced farm managers in the feedlots in Ohio and by pen riders in the feedlot in Amarillo. Lungs were examined at slaughter for evidence of pulmonary lesions.[12]

**Collection of samples**—At the time of arrival at a feedlot (day 0) and on various days after arrival, nasal swab specimens were obtained from the cattle. Samples were obtained from all cattle in each arriving group, including those with signs of respiratory tract disease and those that appeared healthy, using a technique described elsewhere.[11] Serum samples were obtained at time of arrival and again on day 28. [11]

**Enzyme-linked immunosorbent assay to detect bovine coronavirus antigen**—An indirect, double-antibody sandwich antigen-capture ELISA developed by Smith et al[13] for detection of BCV in fecal samples from adult dairy cattle was adapted to detect BCV in supernatant fluids of nasal swab specimens, as described elsewhere.[14] Values for the ELISA were calculated by subtracting the mean absorbance value determined for paired negative-coated wells from the mean absorbance value for paired positive-coated wells. Samples with a resulting absorbance of 0.1 or greater were considered positive for BCV.

**Enzyme-linked immunosorbent assay to detect bovine coronavirus antibodies**—An antibody-detection ELISA developed by Smith et al[15] for detection of enteric BCV was adapted to detect antibodies to BCV in serum samples from feedlot cattle, as described elsewhere.[11]

**Testing for additional pathogens**—Subsets of samples were analyzed for other viruses known to cause respiratory tract disease. Serum samples from cattle at Amarillo in the fall of 1996 were tested, using **virus neutralization (VN)** tests, for antibodies against BHV-1, BVDV, PI-3 virus, and BRSV. Supernatants of nasal swab specimens from cattle at Lucasville in the fall of 1996 were tested, using cell-culture virus isolation, to detect BHV-1, BVDV, and BRSV. Samples from that group of cattle were selected for additional testing because of the high number of cattle with respiratory tract disease as well as the relatively high rate (35.9%) of BCV shedding from the respiratory tract of those cattle.

**Statistical analysis**—Outcomes of interest were treatments for cattle with respiratory tract disease at any time during the period in the feedlot, pulmonary lesions at slaughter, and average daily gain during the period in the feedlot.

Primary independent variables of interest were shedding of BCV via the respiratory tract and seroconversion to BCV during the initial 28 days after arrival at a feedlot. Association of these variables with treatment for cattle with respiratory tract disease and pulmonary lesions at slaughter was assessed, using multivariable logistic regression. Multivariable ANOVA were used to assess the association of the independent variables with average daily gain. Models were constructed by specifying an initial model that included group, BCV shedding, and seroconversion. Effects of potentially confounding variables, including sex, BCV titer at time of arrival, and body weight at entry, then were assessed, using a forward-selection procedure, with a value of $P < 0.10$ necessary for inclusion in the model. The interaction between BCV shedding and seroconversion was tested for inclusion in the model. Separate models were created to assess the effects of titers at time of arrival and seroconversion to BHV-1, BVDV, BRSV, and PI-3 virus among the cattle at Amarillo.

## Results

As reported elsewhere,[11] 68 of 837 (8.1%) cattle surveyed were shedding BCV from the respiratory tract, and 473 of 814 (58%) seroconverted to BCV during the initial 28 days after arrival. During the period in the feedlots, 438 of 814 (54%) cattle from which samples were obtained were treated because of respiratory tract disease (**Table 1**). Although 44 of 68 (64.7%) cattle shedding BCV from the respiratory tract were treated because of respiratory tract disease, only 404 of 769 (52.5%) cattle that were not shedding BCV were treated because of respiratory tract disease. None of the cattle at Jackson, which was 1 of only 2 groups of cattle in which BCV was not isolated, were treated because of respiratory tract disease.

A significant ($P = 0.06$) interaction was detected between respiratory shedding of BCV and seroconversion to the virus (**Table 2**). Titer on day 0 was included in the model to account for cattle that had high titers to BCV at time of arrival. Cattle that shed the virus and seroconverted to BCV by day 28 were the most likely to require treatment because of respiratory tract disease, with a risk 1.6 times (95% **confidence interval [CI]**, 0.79 to 3.41) that for cattle that did not shed the virus or seroconvert to BCV (**Table 3**). These cattle also had the lowest geometric mean antibody titer to BCV on day 0. Cattle that were not shedding

Table 1—Results of a survey of cattle at 3 feedlots in Ohio (Jackson, Lucasville, Wooster) and 1 in Texas (Amarillo) on the incidence of bovine respiratory disease complex (BRDC), treatment, and pulmonary lesions at slaughter

| Location and time | No. of calves | Treated for BRDC | | Pulmonary lesions at slaughter (%) |
|---|---|---|---|---|
| | | No. | % | |
| Lucasville, Spring 1996 | | | | |
|   Lot No. 1 | 69 | 50 | 72.5 | 12 |
|   Lot No. 2 | 70 | 48 | 68.5 | 12 |
|   Lot No. 3 | 105 | 70 | 66.7 | 14 |
| Lucasville, Fall 1996 | | | | |
|   Lot No. 1 | 86 | 48 | 55.8 | 26 |
|   Lot No. 2 | 92 | 40 | 43.5 | 33 |
| Wooster, 1996 | 100 | 58 | 58 | NA |
| Jackson, 1996 | 44 | 0 | 0 | NA |
| Amarillo, 1996 | 109 | 26 | 23.9 | 77 |
| Wooster, 1997 | 162 | 98 | 60.5 | NA |
| **Total** | **837** | **438** | **53.7** | **NA** |

NA = Not available.

Table 2—Results of the final multivariable logistic regression model for estimating the adjusted effects of shedding of bovine coronavirus (BCV) and seroconversion on risk of receiving treatment because of respiratory tract disease

| Variable | Beta | Standard error | Odds ratio | 95% CI | P |
|---|---|---|---|---|---|
| Group | — | — | — | — | < 0.001 |
| Acute BCV titer (per 100-unit change in titer) | −0.01 | 0.01 | 0.99 | 0.97–1.01 | 0.18 |
| BCV shedding | | | | | |
| Yes | −0.9993 | 0.36 | 2.7 | 1.36–5.5 | 0.17 |
| No | 0 | — | 1.0 | — | |
| Seroconversion to BCV | | | | | |
| Yes | −0.6211 | 0.5828 | 1.85 | 0.59–5.88 | 0.87 |
| No | 0 | — | 1.0 | — | |
| Interaction between BCV shedding and seroconversion | 1.1412 | 0.6059 | 3.13 | 0.95–10.3 | 0.06 |

95% CI = 95% Confidence interval. — = Not applicable.

Table 3—Interactive effects of BCV shedding and seroconversion on receiving treatment because of respiratory tract disease

| BCV Status | No. of Cattle | Day 0 GMT | Day 28 GMT | Beta | Standard error | Odds ratio | 95% CI |
|---|---|---|---|---|---|---|---|
| No shedding, no seroconversion | 324 | 879 | 778 | 0 | — | 1.0 | — |
| No shedding, seroconverted | 423 | 92 | 3,497 | −0.5201 | 0.1753 | 0.59 | 0.42–0.84 |
| Shedding, no seroconversion | 19 | 165 | 245 | −0.1420 | 0.505 | 0.86 | 0.33–2.42 |
| Shedding, seroconverted | 49 | 52 | 1,865 | 0.4792 | 0.371 | 1.6 | 0.79–3.41 |

Day 0 = Day of arrival at feedlot. GMT = Geometric mean titer.
*See* Table 2 for key.

Table 4—Results of final logistic regression model for estimating the adjusted effects of BCV shedding and seroconversion on pulmonary lesions evident at slaughter

| Variable | Beta | Standard error | Odds ratio | 95% CI | P |
|---|---|---|---|---|---|
| Group | — | — | — | | < 0.001 |
| BCV shedding | | | | | |
| Yes | −0.79 | 0.34 | 2.2 | 1.12–4.32 | 0.020 |
| No | 0 | — | 1.0 | — | |
| Seroconversion to BCV | | | | | |
| Yes | −0.32 | 0.26 | 1.4 | 0.83–2.28 | 0.222 |
| No | 0 | — | 1.0 | — | |
| Day 0 BCV antibody titer | 0.0001 | 0.0001 | 1 | 0.999–1.00 | 0.26 |

*See* Table 2 for key.

the virus but had seroconverted to BCV were the least likely to require treatment. Cattle that did not shed the virus or mount a detectable immune response to BCV had a slightly higher risk of developing respiratory tract disease than those cattle that shed the virus but did not have increased concentrations of BCV antibodies. In cattle at Amarillo, antibody titers on day 0 were not significantly associated with seroconversion to BHV-1, BVDV, BRSV, or PI-3 virus.

After accounting for the effects of group, we did not detect an association between seroconversion to BCV or geometric mean titer at time of arrival and pulmonary lesions at slaughter (**Table 4**). However, those cattle that shed the virus during the 28-day period in the feedlots were 2.2 times more likely (P = 0.02) to have pulmonary lesions when examined at slaughter than those cattle that did not shed the virus.

An association was not found between the effects of BCV shedding or BCV seroconversion and average daily gain. Neither shedding of BCV nor seroconversion to the virus were predictors of average daily gain throughout the course of the study.

Other respiratory viruses (BHV-1, BVDV, BRSV) were not recovered from the subset of nasal swab specimens obtained from cattle fed at Lucasville during fall 1996, using virus isolation techniques. We did not test for bacterial pathogens. Serum neutralization titers to BHV-1, PI-3 virus, BRSV, and BVDV were available for

the cattle at Amarillo, but, apparently, there was not an interaction with BCV titers, and we did not detect a significant effect for those titers on risk for treatment because of respiratory tract disease or average daily gain.

## Discussion

Bovine coronavirus can be isolated from the respiratory tract of feedlot cattle in various geographic locations in the United States,[12,a,b] and serologic evidence for BCV infections exists in cattle in feedlots in Canada and the United States.[16,a] However, the role of BCV in respiratory tract disease in feedlot cattle remains unclear. In the study reported here, encompassing 837 cattle in 4 feedlots in 2 states, we found evidence of shedding of BCV from the respiratory tract and seroconversion to BCV among these cattle, but we also were able to identify an association between BCV infection and health in these cattle.

Using multivariable logistic regression to assess our data revealed an interaction between shedding of BCV via the respiratory tract and seroconversion to the virus. Therefore, the effects of BCV shedding and seroconversion should not be interpreted independently, because the effect of 1 varied in a manner dependent on the other. Thus, the 2 factors were considered together when analyzing their effect on the risk for developing respiratory tract disease.

It is interesting that cattle that were shedding the virus and seroconverted to BCV during the initial 28 days after arrival were at increased risk for developing respiratory tract disease, compared with cattle that did not shed the virus or seroconvert. Because the majority of viral shedding took place during the first week after arrival, those at-risk cattle were most likely infected prior to arrival and did not mount a protective immune response in time to prevent BCV infection. This relatively small number of cattle introduced the virus to previously unexposed penmates via commingling of cattle from various sources. By the end of the initial 28 days in the feedlots, the majority of cattle had been exposed to the virus and mounted an antibody response against BCV.

Cattle that did not shed the virus from their respiratory tract but did seroconvert had the least risk for requiring treatment because of respiratory tract disease. There are a number of possibilities as to the reason that viral shedding was not detected in these cattle, even though they had serologic evidence of BCV infection. As a result of schedules for sample collection, there may have been brief periods of viral shedding during the interval between sample collections. It also is possible that these cattle were infected with an enteric strain of BCV to which they mounted an antibody response. Previous comparisons of an enteric strain of BCV and a strain of BCV from the respiratory tract found them to be antigenically similar, with 6 of 10 BCV strains in the respiratory tract having similar hemagglutination patterns to those of enteric strains of BCV.[14] It is possible that infection with an enteric strain of BCV provided immunologic crossprotection against infection with a strain of BCV from the respiratory tract.

Another apparent paradox was seen with the 19 cattle that shed the virus but that did not seroconvert to BCV. In addition to the possibilities of false-positive results for the antigen ELISA or false-negative results for the antibody ELISA, it is possible that these cattle had relatively high BCV antibody titers at arrival (mean titer, 165), which were protective. It is also possible that these cattle seroconverted sometime after day 28, the day on which convalescent samples were obtained, or that the cattle were immunosuppressed, which is not an uncommon finding in feedlot cattle.

Although seroconversion to BCV and the BCV antibody titer at time of arrival did not have an apparent effect on pulmonary lesions at slaughter (after accounting for the effect of group), it is interesting that cattle shedding BCV from the respiratory tract were 2.2 times more likely to have lesions at slaughter than cattle not shedding the virus. It appears that detection of BCV during the initial 28 days after arrival at the feedlots was a marker for respiratory tract disease that would be sufficiently severe to cause lesions evident at slaughter.

Shedding of BCV via the respiratory tract or seroconversion did not affect average daily gain. It is expected that most of the effects of infection would be seen during the initial 28 days after arrival, because almost all of the viral shedding was detected during the first week after arrival, predominantly during the first 3 days. By the end of the initial 28 days after arrival, most cattle have been exposed to BCV and developed antibodies to the virus, thus preventing a second infection that could substantially decrease average daily gain after several months at the feedlots. Other investigators[16] also found that seroconversion to BCV was not associated with weight gain but that higher BCV titers on the day of arrival did result in increased weight gain. Such benefits were not found in the study reported here.

In the subset of samples obtained from cattle at Lucasville in fall 1996, other viral pathogens were not recovered. The treatment rate because of respiratory tract disease in this group was 49% (88 of 178), most likely as a result of pneumonia caused by bacteria. Because those cattle were vaccinated against BRSV, BVDV, BHV-1, and PI-3 virus, and those viruses were not isolated from the nasal swab specimens, it is likely that BCV worked synergistically with the bacterial agents and physical stresses to allow bacterial colonization of the lungs of those cattle, leading to pneumonia. With the use of routine vaccination of feedlot cattle against common respiratory tract pathogens, feedlot personnel may be inadvertently selecting for previously unrecognized viral pathogens of the respiratory tract, including BCV.

Although detecting 1 additional factor in the web of BRDC will not prevent the devastation the disease causes, developing additional prevention and control measures could help reduce BRDC. We believe BCV infects cattle in feedlots and apparently increases the risk of cattle in feedlots to develop respiratory tract disease.

[a]Lathrop SL, Wittum TE, Morley PS, et al. Bovine coronavirus respiratory infections in feedlot cattle (abstr), in *Proceedings.* Conf Res Workers Anim Dis 1996;200.

[b]Storz J, Purdy CW, Lin XQ, et al. Market-stressed cattle of a shipping

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