

# The Association of Titers to *Haemophilus somnus*, and other Putative Pathogens, with the Occurrence of Bovine Respiratory Disease and Weight Gain in Feedlot Calves

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## ABSTRACT

Serum samples were obtained from 602 calves (from 19 groups in four feedlots: three in Ontario, and one in Alberta) upon arrival at the feedlot and 28 d later. Of these calves, 202 developed bovine respiratory disease (BRD) and 400 did not develop BRD. Based on high antibody titers noted upon arrival, we infer that most calves were exposed to *Haemophilus somnus* prior to arrival at the feedlot. Within a group, calves with high titers on arrival had a reduced risk of developing BRD later. Most calves did not experience titer increases after arrival; however, calves that had stable or increasing titers had a relatively low risk of contracting BRD. The calves at greatest risk of BRD were those with titers on arrival of less than 6.8 units and subsequent titer decreases of more than 1 unit. The effects of both the titer on arrival and the titer change after arrival were stable when the serologic effects of a number of viruses and *Mycoplasma* agents were considered. Neither antibody titer on arrival nor titer change was related to weight gain differences among calves. Calves with BRD or calves with lower weight on arrival had decreased weight gains in the first 28-day feeding period. The high titers on arrival may have protected most calves against further infection with *H. somnus*. However, since the calves that developed BRD had large titer increases to a number of viruses and to *Pasteurella haemolytica*, while having decreased anti-

body titers to *H. somnus*, we infer that the existing antibodies were "used up" in combatting the agents, including *H. somnus*, which may have "caused" the BRD. Calves which were able to increase their antibody levels to *H. somnus* tended to have a reduced risk of BRD.

## RÉSUMÉ

Des échantillons de sérum ont été obtenus à 2 reprises (à leur arrivée et 28 j plus tard) chez 602 veaux répartis en 19 groupes dans 4 parcs d'engraissement (3 en Ontario et 1 en Alberta). Un total de 202 animaux ont présenté des signes de maladie respiratoire bovine (MRB) alors que les 400 autres animaux ne présentèrent aucun signe. Compte tenu des titres sérologiques notés à l'arrivée des animaux, il semble que la plupart des animaux furent exposés à *Haemophilus somnus* avant leur entrée au parc d'engraissement. À l'intérieur d'un groupe, les animaux possédant des titres élevés à l'arrivée étaient moins à risque de développer une MRB. Après leur arrivée, la majorité des veaux ne présentèrent pas d'augmentation des titres sérologiques; par contre, les veaux dont les titres sériques sont demeurés stables ou légèrement augmentés avaient un risque faible de développer une MRB. Les veaux les plus à risque de MRB étaient ceux dont les titres à l'arrivée étaient inférieurs à 6,8 unités et qui ont eu une diminution subséquente du titre de plus de 1 unité. L'influence du titre sérique à l'arrivée

et le changement de titre après l'arrivée était stable lorsque l'effet de plusieurs virus et mycoplasmes sur la sérologie était pris en considération. Ni le titre d'anticorps à l'arrivée ni le changement de titre n'étaient reliés à des différences de gain de poids parmi les veaux. Les veaux avec MRB ou ceux ayant un poids plus faible à leur arrivée ont eu un gain de poids inférieur durant la période des premiers 28 j. Les titres sérologiques élevés à l'arrivée peuvent avoir protégé la majorité des animaux contre une infection supplémentaire à *H. somnus*. Par contre, étant donné que les veaux ayant présenté une MRB ont démontré une forte augmentation de titre envers plusieurs virus et *Pasteurella haemolytica*, et ont présenté en même temps une diminution du titre envers *H. somnus*, il est supposé que les anticorps présents ont été utilisés pour combattre les agents infectieux, dont *H. somnus*, ce qui aurait entraîné les MRB. Les veaux en mesure d'augmenter leur niveaux d'anticorps contre *H. somnus* étaient moins à risque d'avoir une MRB.

(Traduit par docteur Serge Messier)

## INTRODUCTION

Bovine respiratory disease (BRD) remains a serious health problem in feedlot calves. In Western Canada, *Haemophilus somnus* (HS) has become a frequently stated cause of myocarditis, pneumonia and pleuritis in feedlot cattle, in addition to its more widely known role in arthritis and septicemia (1). In a large

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Saskatchewan feedlot, most of the 874 calves sampled had low antibody titers to *H. somnus* on arrival, but large increases ( $\geq 5\times$ ) in titer by Day 96 (after arrival), from which it was inferred that natural infection was occurring in the feedlot (2). Calves treated for BRD tended to have lower titres ( $P = 0.13$ ) to *H. somnus* on arrival than non-treated calves. Similarly, based on serologic results from a recent incidence density case-control study, in one Alberta feedlot, exposure of calves to *H. somnus* was widespread prior to feedlot entry and, based on titer increases, continued thereafter (3). Calves that subsequently developed BRD (denoted as cases of "fever") tended to have lower titers on arrival than those that did not develop BRD ( $P = 0.103$ ), and by Day 33 in the feedlot, the calves which had developed BRD had smaller titer increases than the control calves (3).

In early experimental work, there did not appear to be a relationship between titer and the response of individual calves ( $n = 5$ ) challenged with *H. somnus* (4). More recently, chronic pneumonia was induced in calves ( $n = 2$ ) by the intrapulmonary injection of  $10^7$  cfu of *H. somnus* and the convalescent serum from these calves later prevented pneumonic changes in the lungs of other calves (5).

Based on the responses to both subcutaneous and intramuscular vaccinations, and the titer differences after arrival (presumably reflecting natural aerosol exposure) at the feedlot, it would appear that calves exposed to *H. somnus* antigens respond in a predictable manner; that is, with a titer increase (5,6). Vaccination against *H. somnus* increased the titers on Days 14 and 28 and reduced the BRD morbidity rate in feedlot calves. *H. somnus* titer on arrival was not associated with subsequent BRD occurrence (6). There was no association between *H. somnus* titers and the occurrence of enzootic pneumonia in calves (7). Titer increases after challenge with *H. somnus* were also observed when pregnant cows and heifers were challenged intravenously or intrabronchially with reproductive tract strains of *H. somnus* (8).

There are no field studies of the frequency of *H. somnus* nor of its association with BRD in feedlot cattle in

Ontario. Therefore the objectives of this study were to examine the potential association of *H. somnus* with BRD and weight gain, both by itself and, in order to prevent confounding, in concert with other putative pathogens in calves in Ontario and Alberta feedlots.

## MATERIALS AND METHODS

Groups of calves were defined as the aggregate of calves that came from different sources or arrived at the specific feedlot on different days. The calves in this study came from 19 groups (Nos. 11, 12, 15 to 21, 33, and 44, in Ontario, and 60 to 67 in Alberta feedlots). The 300 calves in groups 11, 12, and 15 to 21 were fed at the Advanced Agricultural Testing Feedlot in Petersburg, Ontario, during the study years 1991–92. These calves originated from western Canada, Ontario and Quebec, were housed under roof in groups of 6 to 8 per pen, each pen had a concrete floor front and a bedded area at the back. The 120 western Canadian calves, in group 33, were fed at the Elora feedlot in 1990–91. They were housed in groups of 4 to 6, under a roof, on a slatted floor. Initially, the pens were bedded, allowing the calves to acclimatize to the flooring. The 123 western Canadian calves, in group 44, were housed at the Ridgetown feedlot in 1990–91. Calves were housed in groups of approximately 12 calves per pen; all pens were bedded. These calves received a MLV IBR-PIV<sub>3</sub> vaccine on arrival. For the 249 calves in groups 60 to 67, over the period 1990–91, 17 groups of calves were housed at the Advanced Research International (ARI), Airdrie, Alberta feedlot. Two groups (60 and 61) came from Manitoba sales yards, four groups (62 to 64, 67) came from Alberta buyers and two groups (65 and 66) came from Saskatchewan. Calves were housed in groups of 30 or more calves, and, if available, approximately 32 calves (one group had only 25 calves) were bled per group. These calves received a MLV IBR-PI<sub>3</sub> vaccine on arrival. All of the calves in this study were 6–9 mo old at entry to the feedlots. Calves were weighed and had serum samples taken on arrival and at 28 d postarrival.

The disease under consideration was clinical bovine respiratory disease (BRD). Calves were observed daily for the occurrence of signs suggestive of BRD. These signs included one or more of depression, rapid shallow breathing, or being off their feed. Suspected cases were removed from the pen and examined; "sick" calves with no signs referable to body systems other than the respiratory tract were denoted as a case of BRD. Most, but not all, calves with BRD had rectal temperatures greater than 40°C. Calves that were visibly ill on arrival were excluded from the study.

*H. somnus* titers were obtained at the Veterinary Infectious Disease Organization (VIDO) using methods for the outer membrane protein (9). Briefly, the method was as follows: purified *H. somnus* outer membrane proteins were diluted in 50 mM carbonate buffer, pH 9.5, to a final concentration of 10 µg/mL, and 100 µL were added to each well of a 96-well plate (Microtiter Plate, Dynastar Laboratories Immunlon II, Baxter/Canlab, Toronto, Ontario). After 24 h at 4°C, plates were washed 4 times with distilled water and 4-fold serial dilutions of the test sera were made in each row of the antigen plate. Plates were incubated at room temperature for 1 h and washed 8 times in distilled water. The 2nd antibody (goat anti-bovine IgG alkaline phosphatase conjugate, 500 µg/mL; Kirkegaard & Perry Laboratories, Gaithersburg, Maryland, USA) was diluted 7500-fold and 100 µL added to each well. After 1 h, plates were washed 8 times, the substrate was added and the phosphatase activity measured colorimetrically with a commercial ELISA reader (ELISA Amplification System, Gibco/BRL, Mississauga, Ontario). The background was calculated by taking the mean absorbance plus 2 standard deviations of the negative control wells. The endpoint titer of each sample was the final dilution which resulted in a positive value relative to the background, and was expressed as the reciprocal log<sub>4</sub> of the endpoint titer. Suffixes of 0, 28, and D refer to a sample taken on arrival, a sample taken 28 d after arrival, and the difference in titer from Day 0 to Day 28, respectively.

Titer data on other putative pathogens were included in the analyses to

**TABLE I. The BRD and *H. somnus* titer status for calves on arrival and differences in titer after 28 d**

Feedlot location	Variable	Average <i>H. somnus</i> titer			
		<i>n</i>	BRD Positive	<i>n</i>	BRD Negative
Alberta	HS-0	95	7.73 ± 1.96	263	7.85 ± 1.19
	HS-D		-0.62 ± 1.94		-0.33 ± 1.20
Ontario	HS-0	107	7.39 ± 1.1	137	7.32 ± 1.23
	HS-D		-0.08 ± 1.17		0.17 ± 1.14
Overall	HS-0	212	7.57 ± 1.62	490	7.50 ± 1.24
	HS-D		-0.36 ± 0.97		0.07 ± 1.18

prevent confounding of results by other organisms. Indirect agglutination titers to *Pasteurella haemolytica* surface antigens (PhA) and leukotoxin titers (PhL) were obtained (10). Other organisms for which titers were measured included *Mycoplasma bovis* (Mbov) and *Mycoplasma dispar* (Mdis) (11), and five viruses: bovine corona virus (BCV), IBRV, BVDV, PIV-3, and BRSV (12,13).

Statistical analyses were conducted at the calf level. Initial logistic models contained the *H. somnus* titer data on arrival (HS-0), the *H. somnus* titer difference (HS-D), and the location (Province) of the feedlot. Interaction terms between titer on arrival and titer difference and province of feedlot site were evaluated for significance. Then, the provincial location of the feedlot was removed and 18 dummy variables, each denoting one group of calves, were forced into the model along with the titer variables HS-0 and HS-D. Subsequently, models were constructed containing the titer difference between arrival and Day 28 in the feedlot to each of the other putative pathogens, one organism at a time, in addition to the *H. somnus* titer data. The associations of *H. somnus* titer on arrival to rectal temperature at the time of treatment and to the time of developing BRD were evaluated. The shape of the dose-response (titer-BRD risk) curve was evaluated using hierarchical dummy variables (14).

## RESULTS

The calf groups ranged in size from 15 to 123 calves, of which from 14 to 64 individuals were bled to obtain serum samples. Overall there were 602 calves with *H. somnus* titers on arrival; of these, 592 had a recorded titer at Day 28.

On arrival, titers to *H. somnus* of calves in Alberta ( $7.8 \pm 1.57$  (SD),  $n = 244$ ) were slightly higher than in calves from Ontario ( $7.30 \pm 1.20$ ,  $n = 358$ ). The *H. somnus* titers tended to decrease during the first 28 d in Alberta calves ( $-0.46 \pm 1.57$ ) and increased slightly in calves in Ontario ( $0.11 \pm 1.15$ ). The *H. somnus* arrival titer and titer difference by feedlot location and BRD status are shown in Table I. Overall, there was no difference in titer on arrival between calves that later developed BRD and those that did not. Calves that developed BRD had a titer decrease, whereas those that did not develop BRD had a stable titer, or a lesser decrease in titer, in the first 28 d (difference significant  $P < 0.05$ ). By inspection, the relationship of *H. somnus* arrival titer and risk of BRD appeared to follow an inverse linear pattern (calves with higher titers had a lower risk of BRD) for calves in Alberta, but not for calves in Ontario. There was no association between HS-0 and rectal temperature at the time of illness, nor between arrival titer and time, in weeks, of BRD onset.

In the logistic model with BRD at the individual calf level as the outcome (BRD positive = 1), HS-D, but not HS-0, was significantly related to the risk of BRD. When both variables were present in the model, both HS-0 ( $b = -0.26$ ) and HS-D ( $b = -0.42$ ) were related significantly to BRD occurrence. There was no significant interaction between arrival titer and titer difference and BRD occurrence. When the feedlot location (province) was included in the model, it was found that although calves in Ontario feedlots had a significantly lower risk ( $-0.71$ ) of BRD relative to those housed in Alberta, the coefficients for the association of *H. somnus* titers did not change appreciably. The interaction between feedlot location and titer

difference was not significant. With the 18 dummy variables for group, the coefficients for HS-0 and HS-D were both significant at  $-0.29$  (OR = 0.75 for each unit increase) and  $-0.38$  (OR = 0.68 for each unit titer increase), respectively.

The hierarchical dummy variables for titer and titer difference were used to investigate the shape of the dose response curve between *H. somnus* titers and risk of BRD. The cutpoints for the 10th, 25th, 50th, 75th and 90th percentiles of HS-0 were 5.8, 6.8, 7.5, 8.4 and 9.0, respectively. For titer difference they were  $-1.6$ ,  $-0.9$ ,  $-0.1$ ,  $0.6$  and  $1.4$ , respectively. When the sets of hierarchical dummy variables for both titer on arrival and titer difference were present, the statistically significant risk pattern was as follows: calves with a titer on arrival between 6.8 and 9 had a BRD risk of  $0.33\times$  ( $b = -0.59$ ) relative to calves with lower arrival titers; calves with arrival titers of 9 or more had a further reduction in their BRD risk ( $b = -1.13$ ) to  $0.18\times$  relative to those with titers on arrival of less than 6.8; calves with a titer decrease of between less than 1 unit and a titer increase of 0.6 units had a risk of BRD of  $0.45\times$  ( $b = -0.8$ ) while calves with a titer increase of more than 0.6 units had a further decrease in risk of BRD ( $b = -0.5$ ) to  $0.27\times$ , relative to calves with titer changes of more than a 1 unit decrease in titer. The calves at greatest risk of BRD were those with titers on arrival of less than 6.8 units and subsequent titer decreases of more than 1 unit.

Table II contains the summary coefficients for the *H. somnus* titer variables and the titer difference data for each of the selected putative pathogens. It is noteworthy that all variables for titer difference except for IBRV-D, PI3V-D and Mbov-D were significant at the 10% level, and both HS-0 and HS-D variables remained significant ( $P < 0.05$ ) and relatively stable in all models.

The average weight at arrival was  $241.3 \pm 42.8$  kg and ranged from 146 to 345 kg. Calves in the Alberta feedlot were, on average, much heavier on arrival than those in Ontario feedlots, and calves with BRD were heavier than those without BRD. However, within a province, the initial weights, were not significantly different

**TABLE II. Logistic model coefficients for *H. somnus* titers and titer difference to other putative pathogens with BRD as the outcome in feedlot calves**

Other putative pathogen	HS-0 coefficient	HS-D coefficient	Coefficient for other putative pathogen
BCV-D	-0.36	-0.44	0.10
BVDV-D	-0.36	-0.446	0.15
BRSV-D	-0.39	-0.46	0.16
PI3V-D	-0.34	-0.42	0.04 NS
IBRV-D	-0.36	-0.44	0.07 NS
Mbov-D	-0.46	-0.51	-0.05 NS
Mdis-D	-0.46	-0.51	0.09
PhA-D	-0.33	-0.43	0.09
PhL-D	-0.32	-0.41	0.08

All coefficients for putative pathogens, except for those indicated as NS (non-significant), are significant at  $P \leq 0.1$ . All *H. somnus* coefficients are significant at  $P \leq 0.05$

**TABLE III. Weight (kg) on arrival (WT-0) and Day 28 weight gains (WT-D) for feedlot calves by feedlot location and BRD status**

Feedlot location	BRD status	n	WT-0 ( $\pm$ SD)	WT-D ( $\pm$ SD)
Alberta		244	278.41 $\pm$ 19.99	26.87 $\pm$ 12.76
Ontario		358	215.74 $\pm$ 34.74	5.80 $\pm$ 15.64
Overall	Positive	202	248.88 $\pm$ 40.08	11.97 $\pm$ 20.01
	Negative	400	237.24 $\pm$ 43.55	15.55 $\pm$ 16.54
Alberta	Positive	107	278.03 $\pm$ 19.25	22.23 $\pm$ 11.71
	Negative	137	278.72 $\pm$ 20.62	30.48 $\pm$ 12.40
Ontario	Positive	95	216.04 $\pm$ 31.00	0.27 $\pm$ 21.09
	Negative	263	215.63 $\pm$ 36.05	7.78 $\pm$ 12.63

Note: Neither, weight on arrival, nor weight gain were associated with titer to *H. somnus*

between those that developed BRD and those that did not (Table III). Calves in Alberta had a higher mean gain than calves in Ontario, within the provinces, calves with BRD had a lower weight gain than those without BRD. Overall, the weight gains for animals without BRD were significantly higher than those with BRD.

The initial weight (WT-0) was found to be a significant factor ( $P = 0.0022$ ) in predicting the risk of BRD with initial weight as the sole explanatory variable. However, in the model containing both initial weight and location of calves, the location was highly significant with  $P \leq 0.002$  and the effect of initial weight became non-significant, ( $P \geq 0.896$ ). In the model containing initial weight plus HS-0, HS-D and feedlot location, only the location of the feedlot had a significant relationship with weight gain. With weight gain as an outcome, and group effects controlled, in regression analysis, both BRD occurrence ( $b = -8.76$ ) and initial weight ( $b = -0.05$ ) were significant. Neither titer variable for *H. somnus* was significant, regardless of whether the variable for BRD was present in the model or not. The  $R^2$  for the model was 0.51. However most of this association was due to group effects.

## DISCUSSION

Although *H. somnus* is a recognized pathogen of the respiratory system in cattle, the serology of the related disease is only partially understood. Certainly the relationship, if any, between titer and protection remains unknown, and the main reasons for disparate findings have been outlined elsewhere (1). In a stable situation, one would usually interpret a high titer to HS in the absence of disease as being protective against future disease caused by HS, including at least some BRD occurrence. However, in a dynamic situation where calves appear to be exposed to a number of agents in the short time period between weaning and arrival at the feedlot, higher titers could merely indicate an earlier time of infection, or a greater response to infection. Of course lower titers at a given point in time, such as arrival, could reflect an inability of the calf to respond to infection, or just a more recent, or less serious, infection. Titer increases are usually expected after natural or experimental challenge, although it is argued that titer decreases should also be taken as indicative of an active infection which is using up available antibodies faster than they can

develop. In this study we examined titer as both a quantitative as well as a categorical variable. It would appear that the quantitative format is simplest and provides an adequate summary of titer versus BRD risk associations. The significant categorical approach provided stronger measures of association, indicating a nonlinear, but largely monotonic, titer-risk relationship.

In the current study, calves with a relatively high titer ( $\log_4 \geq 6.8$ ) on arrival appeared to be protected against subsequent BRD and this was more pronounced for the calves with very high titers ( $\geq 9$ ). Overall, the arrival titers in the current study were much higher than those noted in a study in Saskatchewan, but are similar to those reported for calves on arrival in a study in Alberta (3). In the recent Alberta incidence density type of case-control study, calves that fit the definition of "fever" on arrival (in a loose sense these calves had what we would denote as BRD with rectal temperature  $\geq 40.3^\circ\text{C}$ ) had *H. somnus* titers that tended to be lower than titers in "control" calves at that point in time (3). Subsequently, at the time of diagnosis "fever" calves had essentially the same titers as control calves. The *H. somnus* titers, on arrival, of calves that died of BRD were significantly lower than the *H. somnus* titers of calves which lived, but there was no difference in arrival titer between calves that subsequently died of *H. somnus* versus those that lived. As noted, in the current study, calves with relatively higher arrival titers, within a group, had a lower subsequent risk of BRD. When both arrival titer and titer increase were included in the same model, because they were both negatively associated with BRD, as well as negatively associated with each other, the strength of association between arrival titer and BRD was increased after control for titer increases. A similar protective trend (non-significant) of higher titers on arrival was noted in the study from Saskatchewan (2).

With regard to titer increases after arrival, in the Alberta case-control study, calves that lived had larger ( $2.9\times$ ) increases in titer than those that died of BRD, but those that died of hemophilosis had similar titer increases to those that lived. At the

time at which the "fever" cases were diagnosed, the control calves usually had similar titers to the cases. By 33 d after arrival, the titer increases in calves which had become cases (2.2×) were significantly lower than the titer increases in calves which remained as controls (3.2×). Except for differences in magnitude of change, these findings agree with those of the current study, in which calves that experienced a relatively large increase in, or stable, titer in the 28 d after arrival, were at decreased risk of BRD. The finding of larger titer increases (or smaller titer decreases) in calves not treated for BRD would superficially lead one to conclude that ability to respond to exposure to *H. somnus* is protective against BRD in most calves. Interestingly, however, calves with BRD appeared to be inhibited in their response to *H. somnus*, but not to other organisms as titer increases to the latter organisms were often large. Recalling that each unit of titer change reflects a 4-fold difference in titer, given the titer increases (or lesser decreases) in control calves, we infer that exposure after arrival was continuing, but may have been relatively limited in the calves in the current study. Another finding of interest in this study was that there were only small titer differences between calves in Alberta and Ontario feedlots, and the relationships of titer difference to BRD occurrence were similar. Thus, if titer reflects exposure, it would seem that the exposure of cattle to *H. somnus* is similar in both locations. This leads to another important question as *H. somnus* has not been deemed to be a major cause of BRD in Ontario. One might speculate therefore that other organisms are necessary to act as components, with *H. somnus*, of a sufficient cause to "trigger" the occurrence of BRD, and these organisms may differ in frequency between western Canadian and Ontario feedlot cattle.

With respect to the possible effects of other organisms, simultaneous recent exposure to most other organisms (as indicated by titer difference), except IBRV, PIV3 and Mbov, added, significantly ( $P \leq 0.1$ ) to the risk of BRD. The coefficients for *H. somnus* were very stable and overall suggest

that for each log<sub>4</sub> unit increase in *H. somnus* titer on arrival, the calves had a decreased BRD risk of 0.7×; calves with a log unit increase in titer after arrival were at 0.65× reduced risk of BRD. Thus the calves that developed BRD tended to be those with a low *H. somnus* titer on arrival and/or those with a titer decrease to *H. somnus* after arrival. If the exposure to *H. somnus* follows a pattern that is similar to that for *P. haemolytica* one would expect exposure to occur during shipment to the feedlot and continue for a few weeks after arrival; normally this would give rise to titer increases regardless of disease status. This could account for the "protection" afforded by titer on arrival. However, if active infection was continuing one might expect larger titer increases than was noted in the current study (more on a par with the findings of the feedlot data from Alberta). Regardless, the calves that developed BRD were those that had decreasing *H. somnus* titers, in both an absolute sense and also relative to the titers of the calves that did not develop BRD. Since all the other organisms that had significant association with BRD had titer increases as a risk factor for BRD, it is difficult to explain the *H. somnus* response, or lack thereof, other than through a "using up of antibody" process or a lack of challenge.

Weight gain, in this study, was largely influenced by initial weight and the occurrence of BRD. *H. somnus* titers appeared to have little influence although the small titer differences after arrival would mitigate against finding a significant relationship. In some senses weight gain can be used as a surrogate for BRD since calves do not eat well while affected with BRD. However, despite the association of titers with BRD occurrence, there was no association with weight gain, whether the effects of BRD were controlled or not. This might indicate that the cases of BRD which might be causally related to *H. somnus* were principally the less severe cases of BRD. Clearly, much more work needs to be done to understand the serology of BRD as it relates to *H. somnus* exposure and protection against BRD, and reduced weight gains.

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