ELSEVIER
SAUNDERS

Vet Clin Food Anim 20 (2004) 39–50

VETERINARY
CLINICS
Food Animal Practice

Effect of bovine viral diarrhea virus in the feedlot

John R. Campbell, DVM, DVSc

Department of Large Animal Clinical Sciences, Western College of Veterinary Medicine, University of Saskatchewan, 52 Campus Drive, Saskatoon, Saskatchewan, Canada

It could be argued that bovine viral diarrhea virus (BVDV) is one of the most economically significant infectious pathogens of feedlot cattle. Although the direct economic losses caused by this virus have not been well quantified, the role it plays as an immunosuppressive agent and as a potentiator for other diseases, most notably bovine respiratory disease, have been well documented. It is also a difficult disease for the feedlot veterinarian to control effectively. Individual cattle persistently infected (PI) with BVDV often serve as the source of infectious virus within a group of feedlot cattle, and the ultimate responsibility for preventing persistent infections in cattle rests with the cow-calf producer and not with the feedlot owner. The enormous impact of the virus on the livestock industry has led the Academy of Veterinary Consultants to draft a position statement that resolves that the beef and dairy industries adopt measures to control and target eventual eradication of BVDV from North America [1].

Persistently infected calves in the feedlot

There is little doubt about the importance of the PI cattle with respect to the epidemiology and transmission of BVDV in cattle populations [2–5]. Cattle that are PI with BVDV shed copious amounts of virus into their environment [6]. PI animals are a major source of virus among newly arrived feedlot cattle, and pose a significant threat for spreading the virus and establishing acute or primary infections in naïve cattle [2,4,5,7,8]. PI calves tend to have lower growth rates [4,9], and often die from classic mucosal disease or other diseases during the feeding period [4].

Feedlot veterinarians who perform routine necropsies will sometimes identify PI calves at necropsy that have classical lesions of mucosal disease.

E-mail address: john.campbell@usask.ca

doi:10.1016/j.cvfa.2003.11.003

Unpublished observations have shown these cases to be clustered approximately 2 weeks after arrival in feedlots where modified live BVDV vaccines are used leading to speculation that the vaccine may play a role of precipitating mucosal disease in some cases of PI calves. However, this has not been documented conclusively in the scientific literature, although instances of postvaccinal mucosal disease have been reported [10,11].

Taylor et al [4] purchased 28 PI calves from a cow-calf operation and placed them in a pen by themselves in a commercial feedyard. The majority of the PI calves were unthrifty at weaning, and had an adjusted weaning weight which was 43 kg lower on average than non-PI calves. Twenty-four of the 28 PI calves died during the feeding period and four of the PI calves survived until slaughter. Approximately 25% of the calves had evidence of pneumonic lesions at necropsy, and the authors noted that the possibility of misdiagnosing the calves as something other than mucosal disease on the basis of gross necropsy was a significant possibility in some of the cases.

The prevalence of PI calves in feedlot populations has not been well established. One estimate of the prevalence of PI calves in a single feedlot in Western Canada found less than 0.1% of calves PI with BVDV [12]. Bolin et al estimated the prevalence of PI calves in the population at approximately 1.7%, although this sample of 3157 cattle from 66 herds included calves and adult cattle from both beef and dairy herds [13]. A mathematical model of BVDV infection dynamics predicted a prevalence of 1.2% PI animals, and this prevalence was fairly insensitive to alterations of parameter values [14]. A sample of 18,931 calves from 128 U.S. beef herds revealed that 4% of randomly selected herds had PI calves present in them [2]. Herds that were suspected of having BVDV infections based on clinical signs were more likely to have a PI calf present. Nineteen percent of these herds were found to have PI calves present [2]. This study also demonstrated that the majority of these PI calves survived until weaning, which would allow them to arrive at the feedlot as a major source of BVDV [2].

Despite the relatively low estimated overall prevalence of PI cattle, it is probable that PI cattle can cluster within certain groups or pens at the feedlot. Several studies have reported that the presence of multiple PI calves clustered within herds [2,4,8,9,13]. The synchronized nature of the cow-calf breeding cycle would make multiple persistent infections common in infected beef herds. As well, sorting groups of cattle by weight throughout the auction market system and in the feedlot may concentrate those PI calves that tend to have poor growth rates into the groups of cattle with lighter arrival weights [4].

Acute or primary bovine viral diarrhea virus infections

The loss of a few PI calves due to mucosal disease is probably not of major significance in the overall economic picture of a feedlot operation. The primary concern with PI calves is the fact that they are a source of

BVDV for naïve cattle in the feedlot. Primary or acute infections of BVDV in feedlot cattle play an important role as an immunosuppressive agent or as a potentiator for other diseases [4,5]. Although the majority of acute infections with BVDV are subclinical, acute infections of BVDV are also occasionally identified as a primary cause of mortality of feedlot calves. Recently, clinically severe acute infections of BVDV have been identified in Canada, Great Britain, and the United States [15–17]. Clinical signs of acute BVDV infection may include fever, diarrhea, rapid respiration, inappetance, depression, lymphopenia, and thrombocytopenia [15]. Outbreaks attributed to acute BVDV infections in feedlot calves have been described previously, although definitive diagnosis is often difficult [18]. The immune response of the immunocompetent animal may make recovery of the virus unlikely, and diagnosis must rely on immunohistochemistry or on titer responses [18,19].

The thrombocytopenic manifestation of acute BVDV has been described by a number of authors [17,20,21]. Outbreaks of this form of acute BVDV has been described in groups of feedlot cattle, and is characterized by depression, fever, diarrhea, hemorrhage into the anterior chamber of the eye, epistaxis, bleeding subcutaneously, and bleeding from injection sites [18,22]. Common necropsy findings include extensive ecchymotic hemorrhages on serosal surfaces and evidence of hemorrhage in muscle and between fascial planes [22].

An exceptionally virulent form of acute BVDV infection has also been reported, and although the majority of these reports are in dairy cattle [15–17], this syndrome has also been reported in feeder cattle [15]. Fever, pneumonia, diarrhea, abortions, and sudden death occurred in all ages of cattle, and the gross lesions in the digestive tract were similar to those described for mucosal disease [15,23].

Although acute BVDV infections can present with fulminating and fatal disease, the majority of these infections are inapparent or subclinical [23]. The profound immunosuppressive effects of acute BVDV infections have been well documented and reviewed elsewhere [24,25]. These immunosuppressive effects of acute BVDV infection are responsible for the potentiation of a variety of diseases in cattle including salmonellosis, rotavirus, and coronavirus infections, bovine popular stomatitis, and *Escherichia coli* [24]. However, in feedlot cattle, the potentiation of bovine respiratory disease by BVDV is of primary significance.

Bovine viral diarrhea virus and respiratory disease

Bovine respiratory disease is reported to be the most economically important disease of beef cattle [26]. The role that BVDV plays in respiratory disease of feedlot cattle has been examined extensively in both experimental and epidemiologic studies, and has been reviewed previously [24,27]. The earliest scientific publications that first described BVDV in

North American cattle described a significant respiratory component to the infections [28].

The role of BVDV as a primary respiratory pathogen remains controversial [27]. Potgeiter et al demonstrated in experimental studies that mild clinical respiratory disease and interstitial pneumonia could be induced in 4- to 6-month-old calves inoculated with BVD virus [29]. Potgeiter et al also demonstrated variation in the pneumopathogenicity between various isolates of BVDV [30]. Calves infected with strain 72 demonstrated more severe respiratory symptoms than calves infected with strain 2724 following an inoculation with *Mannheimia haemolytica*. However, it seems unlikely that BVDV plays a major role as a primary respiratory pathogen. The vast majority of the published evidence demonstrates BVDV's role in immunosuppression and its synergistic effects with other infectious agents in feedlot cattle. Many studies have demonstrated the synergistic effects of BVDV with other pathogens. Calves initially inoculated with BVDV before IBR virus infections have a much wider distribution of IBR virus, than calves inoculated with IBR virus alone [29]. The synergistic effects of BVDV and *M hemolytica* have also been demonstrated in experimental models [29,30]. Several studies have demonstrated that BVDV also potentiates the effects of BRSV in calves [31–33]. BVDV was also identified as a frequent viral agent in respiratory disease outbreaks in Quebec in which multiple viral infections were identified [34]. A recent feedlot necropsy study using immunohistochemical staining [35] showed BVDV in the tissues of 13 of 35 calves (37%) dying of pneumonia compared with 4 of 92 calves (4.3%) dying of myocarditis and in 0 of 45 calves (0%) dying of noninfectious causes [36].

Circumstantial evidence has also linked BVDV virus to other important feedlot pathogens such as *Mycoplasma bovis*. *M bovis* has been implicated as an etiologic agent of a chronic pneumonia of feedlot cattle that does not respond to antibiotic therapy, which is often accompanied by a concurrent polyarthritis. Haines et al sampled 49 feedlot animals with chronic unresponsive disease and used immunohistochemical staining to identify antigens of *M bovis, Haemophilus somnus, M hemolytica*, and BVDV. Mycoplasma bovis was demonstrated in over 80% of the cases, and was the only bacterial agent identified in the joints with arthritis. BVDV was identified in 40% of the cases by immunohistochemistry of samples of lung and joint synoviae [37]. Shahriar et al examined a similar series of cases of chronic pneumonia from Western Canadian feedlot cattle and demonstrated BVDV in 62.5% of the cases by using immunohistochemical staining of the heart and lung tissue. The immunohistochemical staining of BVDV was noted to be in association with microscopic vascular lesions in these tissues [38]. In an observational study in a single commercial feedlot, Pollock et al demonstrated that these chronic cases of *Mycoplasma pneumonia* and arthritis were a significant cause of mortality in the feedlot, and that chronic calves with high titers to BVDV were 4.5 times more likely to have polyarthritis than calves with lower titers to BVDV [39].

There have been a significant number of epidemiologic studies that have implicated BVDV as a significant component of the bovine respiratory disease complex [40–48]. In many of these studies the presence of a titer on arrival decreased the subsequent risk of treatment for respiratory disease. As well, in the majority of these studies, seroconversion to BVDV after arriving at the feedlot was associated with an increased risk of treatment for respiratory disease. These studies are summarized in Table 1; however, the reader should be aware that comparing serologic tests between studies is fraught with difficulty, and that the definitions for seropositivity and for seroconversion may also differ between studies.

Martin and Bohac followed 322 Ontario feedlot calves in two small pen research feedlots for the first 28 days of the feeding period 55.8% of the calves had titers to BVDV upon arrival to the feedlots although the presence of a titer on arrival was not associated with BRD risk [40]. Seroconversion to BVDV was shown in 24% of the calves, and this was positively associated with treatment for respiratory disease [40]. Martin et al performed a case control study in 15 groups of feedlot calves in Ontario. Thirty-two percent of the animals that were treated for respiratory disease had titers to BVDV on arrival, while 42% of the controls had positive titers on arrival. Positive titers were associated with a decreased risk for respiratory disease treatment. Forty-two percent of the cases seroconverted during the first 28 days of the feedlot compared with 33% of the controls. Seroconversion to BVDV was shown to be significantly associated with the risk of treatment for respiratory disease [41]. Durham and Hassard followed 283 bull calves in a Western Canadian bull test station. Positive titers were identified in 21% of the bulls on arrival to the test station, and these calves were less likely to be treated for respiratory disease. Only 13% of the bulls seroconverted, and this was not associated with an increased risk of respiratory disease [42]. Allen et al performed a case-control study where acute and convalescent serum samples were taken from 59 cases of BRD and 60 normal animals in a small pen research feedlot in Ontario. In that study, 51% of both the cases and controls seroconverted to BVDV, and there was no associated with seroconversion and treatment [43]. In 1999, Martin et al serologically examined 700 calves from 32 groups in Ontario and Alberta feedlots. Positive arrival titers were identified in 24%, and these animals were 0.9 times as likely to be treated for respiratory disease as calves with no titer on arrival. Fifty percent of the calves in this study seroconverted to BVDV, and these animals were 1.14 times more likely to be treated for respiratory disease. The authors also noted that BVDV had the most consistent relationship with the risk of respiratory disease as well as lower weight gains [44]. Booker et al performed a case-control study of 100 cases of respiratory disease and 100 control animals in a 22,000 head commercial feedlot in Alberta [45]. The percentage of animals with positive titers on arrival, and the percentage of animals that seroconverted could not be determined from this case-control study but the authors clearly demonstrated that treatment for respiratory disease was significantly

Table 1
A summary of sero-epidemiologic studies that have examined the relationship between bovine viral diarrhea virus and bovine respiratory disease in feedlot cattle

Authors	Population studied	% of cattle seropositive to BVDV on arrival	Was arrival titer associated with decreased BRD risk?	% of cattle seroconverting to BVDV virus	Was seroconversion associated with increased BRD risk?
Martin et al 1986 [40]	322 calves, Small pen research feedlots in Ontario	55.8%	No	24%	Yes
Martin et al 1989 [41]	279 cases of BRD and 290 controls from small pen research feedlots in Ontario	32% in cases 42% in controls	Yes	42% in cases 33% in controls	Yes
Durham et al 1991 [42]	283 bull calves at Saskatchewan bull test station	21%	Yes	13%	No
Allen et al 1992 [43]	59 cases of BRD and 60 controls from small pen research feedlot in Ontario	Not applicable	N/A	51%	No
Martin et al 1999 [44]	700 calves from 32 groups from feedlots in Ontario and Alberta	24%	Yes	50%	Yes
Booker et al 1999 [45]	200 head case control study from 22,000 head commercial lot in Alberta	Not calculated	Yes	Not calculated	Yes
Fulton et al 2000 [46]	120 Tennessee calves shipped to Texas	18.3% BVDV type 1 13.3% BVDV type 2	N/A virtually all calves treated	38.5% BVDV type 1 27.9% BVDV type 2	N/A
O'Connor et al 2001 [47]	852 calves from 3 Ontario feedlots	39%	Yes	45%	Yes
Fulton et al 2002 [48]	Two groups of calves: 205 calves and 120 calves from Tennessee	23.1–34.2% BVDV type 1a 17.4–20.0% BVDV type 2	Not calculated	Sick calves: 32.8–47.5% BVDV 1a Healthy calves: 16–28.4% BVDV 1a	Yes

associated both with lower titers to BVDV on arrival and to seroconversion to BVDV during the feeding period [45]. Fulton et al investigated a group of stocker calves suffering from an outbreak of acute respiratory disease after transport from Tennessee auctions to a west Texas feedyard [46]. Associations of titers to various pathogens and respiratory disease could not be determined because the vast majority of the 120 calves (87.5%) were treated for respiratory disease. The authors demonstrated that 18.3% and 13.3% of the calves had antibody titers to BVDV type I and BVDV type II, respectivelym on arrival to the feedyard. Seroconversion was identified in 38.5% and 27.9% of the calves to type I and type II BVDV, respectively [46]. O'Connor et al performed a longitudinal observational study on 852 calves from three Ontario feedlots [47]. Blood samples were collected from the calves on day 0 and day 28 of the feeding period. Thirty-nine percent of the calves were seropositive on arrival and these calves were 0.6 times less likely to be treated for respiratory disease. Seroconversion to BVDV was demonstrated in 45% of the calves, and the calves that seroconverted were 2.02 times more likely to be treated for respiratory disease [47]. Fulton et al followed two groups of stocker calves from Tennessee into feedlots in New Mexico and Texas in 1999 and 2000. Blood samples were collected at weekly intervals for approximately the first 4 weeks of the feeding period. 23.1% and 34.2% of the calves had positive titers for BVDV type 1a and 18.4% and 20.0% of the calves had positive titers for BVDV type 2 on arrival. BVDV1a seroconversions occurred in 47.5% of the sick calves and in 28.4% of the healthy calves, which was a statistically significant difference in the 1999 study. BVDV1a seroconversions occurred in 32.8% of the sick calves and in 16.0% of the healthy calves in the 2000 study. This difference was also statistically significant [48].

The weight of evidence from this group of sero-epidemiologic studies shows that BVDV is consistently associated with respiratory disease in feedlot calves. Calves that arrive at the feedlot with titers to BVDV tend to protective against the risk of respiratory disease, and calves that seroconvert to BVDV during the feeding period are more likely to be treated for respiratory disease. This relationship is relatively consistent throughout all the studies despite variations in serologic testing procedures, timing of bleeding, case definition of positive titers and seroconversion, and case definitions of respiratory disease. It would appear obvious that control of BVDV in beef cattle should play a significant role in prevention of undifferentiated respiratory disease as well as other infectious pathogens in feedlot cattle.

Vaccination for bovine viral diarrhea virus at the feedlot

There is a lack of scientific literature examining the effects of BVDV vaccination on subsequent health parameters of feedlot cattle. A review of bovine respiratory disease vaccine efficacy concluded that there were no

reliable reports of field trials examining the clinical effects of BVDV vaccines in North American feedlot cattle [49]. Shunicht et al performed a clinical field trial in commercial feedyards comparing a multivalent viral vaccine containing modified live infectious bovine rhinotracheitis virus, para-influenza-3 virus, BVDV, and bovine respiratory syncytial virus with a univalent vaccine containing modified live IBR virus [50]. The study was somewhat unique in the fact that pens of cattle were randomized to treatment groups rather than individual animals within pens. This design allows the investigators to examine the effects of the vaccine on feed efficiency as well as eliminating the herd effect of immunity which may diminish significant results. The results demonstrated that those cattle receiving the multivalent vaccine had significantly lower treatment rates in the multivalent vaccine group (16.8% versus 21.7%). As well, cattle receiving the multivalent vaccine had significantly higher carcass weights, weight gain, and average daily gain throughout the feeding period. An economic analysis in the study concluded that there was a net advantage of $0.74 CDN/animal by using the multivalent vaccine [50]. Although the inclusion of modified live BVDV in the multivalent vaccine may have accounted for some of these differences, it was impossible to determine which of the viral components of the multivalent vaccine were responsible for this apparent advantage.

The benefits of prevaccination and preweaning or preconditioning have been demonstrated in a variety of studies and have been reviewed elsewhere [51]. However, it is impossible to separate the effect of BVDV vaccination from the other vaccines and management procedures in these studies [49]. The use of BVDV vaccines before arrival at the feedlot has not been examined specifically. The current promotion of prevaccination may help to improve BVDV immunity upon arrival to the feedlot however, the effect of prevaccination on BVDV immunity has not been well established, and will require further research.

Control of bovine viral diarrhea virus in feedlot cattle

Vaccination on arrival with BVDV vaccines is currently the primary method with which feedlot producers attempt to control the transmission of acute BVDV infections. In the 1999 National Animal Health Monitoring System survey of feedlots, 94.4% of operations used BVDV vaccines and it was estimated that 87.7% of cattle received those vaccines [52]. This was up from the 1994 NAHMS study, which estimated that 87.5% of feedlots were using BVDV vaccines [53]. Despite the high proportion of cattle being given BVDV vaccines, BVDV remains an important problem in feedlot cattle. This may be due to the genetic diversity of the virus, which has been well documented, and the difficulty of vaccinating for all the various genotypes of the virus [48,54,55]. A field trial on calfhood vaccination for bovine viral

diarrhea virus in dairy heifers in drylot conditions similar to feedlot cattle only demonstrated 48% protection [56]. It may also be due to the fact of significant transmission of the virus when cattle are mixed, which occurs during time spent in the auction market system during transport to the feedlot before vaccination and in the feedlot itself before the time in which immunity is induced.

Ultimately, control of this pathogen will rest with the cow-calf industry. The use of prebreeding vaccines with modified live vaccines that can demonstrate fetal protection will be the most significant tool currently available to eliminate the presence of PI calves. As well, effective BVDV biosecurity programs that effectively identify and remove PI cattle from herds and prevent their introduction will be critical [57]. The widespread availability of immunohistochemical tests for BVDV will provide a sensitive means for which to accomplish this goal [19,58]. Voluntary BVDV eradication programs and herd certification programs could give feedlot operators a source of calves that could be at a lower risk for containing PI calves. In combination with prevaccination programs, these types of efforts may provide an opportunity to decrease the effect BVDV plays in infectious disease of feedlot cattle.

References

[1] Groteluesche D. Position statement on bovine viral diarrhea virus: Academy of Veterinary Consultants. In: Detecting and controlling BVDV infections proceedings. Ames (IA); 2002. p. 22.
[2] Wittum TE, Groteluesche DM, Brock KV, Kvasnicka WG, Floyd JG, Kelling CL, et al. Persistent bovine viral diarrhoea virus infection in US beef herds. Prev Vet Med 2001;49: 83–94.
[3] Radostits OM, Littlejohns IR. New concepts in the pathogenesis, diagnosis and control of diseases caused by the bovine viral diarrhea virus. Can Vet J 1988;29:513–28.
[4] Taylor LF, Janzen ED, Ellis JA, van den Hurk JV, Ward P. Performance, survival, necropsy, and virological findings from calves persistently infected with the bovine viral diarrhea virus originating from a single Saskatchewan beef herd. Can Vet J 1997;38: 29–37.
[5] Houe H. Epidemiology of bovine viral diarrhea virus. Vet Clin North Am Food Anim Pract 1995;11:521–47.
[6] McClurkin AW, Littledike ET, Cutlip RC, Frank GH, Coria MF, Bolin SR. Production of cattle immunotolerant to bovine viral diarrhea virus. Can J Comp Med 1984;48:156–61.
[7] Houe H. Epidemiological features and economical importance of bovine virus diarrhea virus infections. Vet Microbiol 1999;64:89–107.
[8] Holland RE, Bezek DM, Sprecher DJ, Patterson JS, Steficek BA, Trapp AL. Investigation of an epizootic of bovine viral diarrhea virus infection in calves. J Am Vet Med Assoc 1993; 202:1849–54.
[9] Kelling CL, Stine LC, Rump KK, Parker RE, Kennedy JE, Stone RT, et al. Investigation of bovine viral diarrhea virus infections in a range beef herd. J Am Vet Med Assoc 1990; 197:589–93.
[10] Bittle JL. Field use of bovine vaccines. J Dairy Sci 1970;53:625–7.
[11] Peter C, Tyler D, Ramsey F. Characteristics of a condition following vaccination with bovine viral diarrhea vaccine. J Am Vet Med Assoc 1967;150:46.

[12] Taylor LF, Van Donkersgoed J, Dubovi EJ, Harland RJ, van den Hurk JV, Ribble CS, et al. The prevalence of bovine viral diarrhea virus infection in a population of feedlot calves in Western Canada. Can J Vet Res 1995;59:87–93.
[13] Bolin SR, McClurkin AW, Coria MF. Frequency of persistent bovine viral diarrhea virus infection in selected cattle herds. Am J Vet Res 1985;46(11):2385–7.
[14] Cherry BR, Reeve MJ, Smith G. Evaluation of bovine viral diarrhea virus control using a mathematical model of infection dynamics. Prev Vet Med 1998;33:91–108.
[15] Carman S, van Dreumel T, Ridpath J, Hazlett M, Alves D, Dubovi E, et al. Severe acute bovine viral diarrhea in Ontario, 1993–1995. J Vet Diagn Invest 1998;10:27–35.
[16] David GP, Crawshaw TR, Gunning RF, Hibberd RC, Lloyd GM, Marsh PR. Severe disease in adult dairy cattle in three UK dairy herds associated with BVD virus infection. Vet Rec 1994;134:468–72.
[17] Rebuhn WC, French TW, Perdrizet JA, Dubovi EJ, Dill SG, Karcher LF. Thrombocytopenia associated with acute bovine virus diarrhea infection in cattle. J Vet Intern Med 1989;3:42–6.
[18] Janzen ED, Clark EG. The diagnosis of BVD outbreaks in Western Canada. In: Proceedings of the international symposium on bovine viral diarrhea virus. Cornell; 1996. p. 143–58.
[19] Dubovi EJ. Laboratory diagnosis of bovine viral diarrhea virus infections. Vet Med 1996; 867–72.
[20] Corapi WV, Elliott RD, French TW, Arthur DG, Bezek DM, Dubovie EJ. Thrombocytopenia and hemorrhages in veal calves infected with bovine viral diarrhea virus. J Am Vet Med Assoc 1990;196:590–6.
[21] Corapi WV, French TW, Dubovi EJ. Severe thrombocytopenia in young calves experimentally infected with noncytopathic bovine viral diarrhea virus. J Virol 1989;63: 3934–43.
[22] Janzen ED, Clark EG. Thrombocytopenia in weaned beef calves. Can Vet J 1995;36:45–6.
[23] Baker JC. The clinical manifestations of bovine viral diarrhea infection. Vet Clin North Am Food Anim Pract 1995;11(3):425–45.
[24] Grooms DL. Role of bovine viral diarrhea virus in the bovine respiratory disease complex. Bovine Practitioners 1998;32:7–12.
[25] Potgieter LND. Immunology of bovine viral diarrhea virus. Vet Clin North Am Food Anim Pract 1995;11(3):501–20.
[26] Griffin D. Economic impact associated with respiratory disease in beef cattle. Vet Clin North Am Food Anim Pract 1997;13(3):367–78.
[27] Potgieter LND. Bovine respiratory tract disease caused by bovine viral diarrhea virus. Vet Clin North Am Food Anim Pract 1997;13(3):471–82.
[28] Olafson O, MacCallum AD, Fox FH. An apparently new transmissible disease of cattle. Cornell Vet 1946;36:205–13.
[29] Potgieter LND, McCracken MD, Hopkins FM, Walker RD, Guy JS. Experimental production of bovine respiratory tract disease with bovine viral diarrhea virus. Am J Vet Res 1984;45:1582–5.
[30] Potgieter LND, McCracken MD, Hopkins FM, Guy JS. Comparison of the pneumopathogenicity of two strains of bovine viral diarrhea virus. Am J Vet Res 1985;46:151–3.
[31] Pollreisz JH, Kelling CL, Brodersen BW, Perino LJ, Cooper VL, Doster AR. Potentiation of bovine respiratory syncytial virus infection in calves by bovine viral diarrhea virus. Bovine Practitioners 1997;31:32–8.
[32] Lehmkuhl HD, Gough PM. Investigation of causative agents of bovine respiratory tract disease in a beef cow–calf herd with and early weaning program. Am J Vet Res 1977;38: 1717–20.
[33] Liu L, Lehmkuhl HD, Kaeberle ML. Synergistic effects of bovine respiratory syncytial virus and non-cytopathic bovine viral diarrhea virus infection on selected bovine alveolar macrophage functions. Can J Vet Res 1999;63(1):41–8.

[34] Richer L, Maois P, Lamontagne L. Association of bovine viral diarrhea virus with multiple viral infections in bovine respiratory disease outbreaks. Can Vet J 1988;29:713–7.
[35] Haines DM, Clark EG, Dubovi EJ. Monoclonal antibody-bsed immunohistochemical detection of bovine viral diarrhea virus in formalin-fixed paraffin-embedded tissues. Vet Pathol 1992;29:27–32.
[36] Haines DM, Moline KM, Sargent RA, Campbell JR, Myers D, Doige P, Immunohistochemical study of Hemophilus somnus, *Mycoplasma bovis*, *Mannheimia hemolytica* and bovine viral diarrhea virus in death losses due to myocarditis in feedlot cattle. Can Vet J (In press).
[37] Haines DM, Martin KM, Clark EG, Jim GK, Janzen ED. The immunohistochemical detection of a high prevalence of *Mycoplasma bovis* and bovine viral diarrhea virus in tissues of feedlot cattle with chronic, unresponsive respiratory disease and/or arthritis. Can Vet J 2001;42:857–60.
[38] Shahriar FM, Clark EG, Janzen E, West K, Wobeser G. Coinfection with bovine viral diarrhea virus and *Mycoplasma bovis* in feedlot cattle with chronic pneumonia. Can Vet J 2002;43:863–8.
[39] Pollock CM, Campbell JR, Janzen ED, West K. Descriptive epidemiology of chronic disease of calves in a western Canadian feedlot. AABP Proc 2000;13:152–3.
[40] Martin SW, Bohac JE. The association between serological titers in infectious bovine rhinotracheitis virus, bovine virus diarrhea virus, parainfluenza-3 virus, respiratory syncytial virus and treatment for respiratory disease in Ontario feedlot calves. Can J Vet Res 1986;50:351–8.
[41] Martin SW, Bateman KG, Shewen PE, Rosendal S, Bohac JE. The frequency, distribution and effects of antibodies to seven putative respiratory pathogens, on respiratory disease and weight gain in feedlot calves in Ontario. Can J Vet Res 1989;53:355–62.
[42] Durham PJK, Hassard LE, Van Donkersoed J. Serological studies of infectious bovine rhinotracheitis, parainfluenza 3, bovine viral diarrhea, and bovine respiratory syncytial viruses in calves following entry to a bull test station. Can Vet J 1991;32:427–9.
[43] Allen JW, Viel L, Bateman KG, et al. Serological titers to bovine herpesvirus 1, bovine viral diarrhea virus, parainfluenza 3 virus, bovine respiratory syncytial virus and Pasturella haemolytica in feedloct calves with respiratory disease: Association with bacteriological and pulmonary cytological values. Can J Vet Res 1992;52:26–33.
[44] Martin SW, Nagy E, Armstrong D, Rosendal S. The associations of viral and mycoplasmal antibody titers with respiratory disease and weight gain in feedlot calves. Can Vet J 1999; 40:560–70.
[45] Booker CW, Guichon PT, Jim GK, Schunicht OC, Harland RJ, Morley PS. Seroepidemiology of undifferentiated fever in feedlot calves in western Canada. Can Vet J 1999;40:40–8.
[46] Fulton RW, Purdy CW, Confer AW, Saliki JT, Loan RW, Briggs RE, et al. Bovine viral diarrhea viral infections in feeder calves with respiratory disease: interactions with *Mannheimia* spp., parainfluenza-3 virus and bovine respiratory syncytial virus. Can J Vet Res 2000;64:151–9.
[47] O'Connor A, Martin SW, Nagy E, Menzies P, Harland R. The relationship between the occurrence of undifferentiated bovine respiratory disease and titer changes to bovine coronavirus and bovine viral diarrhea virus in 3 Ontario feedlots. Can J Vet Res 2001;65: 137–42.
[48] Fulton RW, Ridpath JF, Saliki JT, Briggs RE, Confer AW, Burge LJ, et al. Bovine viral diarrhea virus (BVDV) 1b: predominant BVDV subtype in calves with respiratory disease. Can J Vet Res 2002;66:181–90.
[49] Perino LJ, Hunsaker BD. A review of bovine respiratory disease vaccine field efficacy. Bovine Practitioners 1997;31:59–66.
[50] Schunicht OC, Booker CW, Jim GK, Guichon PT, Wildman BK, Hill BW. Comparison of a multivalent viral vaccine program versus a univalent viral vaccine program on animal

health, feedlot performance, and carcass characteristics of feedlot calves. Can Vet J 2003; 44:43–50.
[51] Cole NA. Preconditioning calves for the feedlot. Vet Clin North Am Food Anim 1985;1(2): 401–11.
[52] National Animal Health Monitoring System. Baseline reference of feedlot health and health management 1999. USDA; 2000.
[53] National Animal Health Monitoring System. Feedlot health management report. Cattle on feed evaluation. USDA; 1994.
[54] Bolin SR, Littledike ET, Ridpath JF. Serologic detection and practical consequences of antigenic diversity among bovine viral diarrhea viruses in a vaccinated herd. Am J Vet Res 1991;52:1033–7.
[55] Ridpath J, Bovine viral diarrhea virus types 1 and 2, Detection and vaccination. In: United States Animal Health Association Proceedings; 1998. p. 1–10.
[56] Callan RJ, Garry FB. Biosecurity and bovine respiratory disease. Vet Clin North Am Food Anim Pract 2002;18(1):57–78.
[57] Njaa BL, Clark EG, Janzen E, Ellis JA, Haines DM. Diagnosis of persistent bovine viral diarrhea virus infection by immunohistochemical staining of formalin-fixed skin biopsy specimens. J Vet Diagn Invest 2000;12:393–9.
[58] Van Donkersgoed J, van den Hurk JV, McCartney D, Harland RJ. Comparative serological responses in calves to eight commercial vaccines against infectious bovine rhinotracheitis, parainfluenza-3, bovine respiratory syncytial, and bovine viral diarrhea viruses. Can Vet J 1991;32:727–33.