Review Article Compte rendu

The epidemiology of bovine respiratory disease: What is the evidence for predisposing factors?

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Abstract — Bovine respiratory disease (BRD) is the most costly disease of beef cattle in North America. It is multi-factorial, with a variety of physical and physiological stressors combining to predispose cattle to pneumonia. However, efforts to discern which factors are most important have frequently failed to establish definitive answers. Calves are at highest risk shortly after transport. Risk factors include purchasing from sale barns and commingling. It is unclear whether or not these practices increase susceptibility, increase exposure, or are proxies for poor management. Lighter-weight calves appear to be at greater risk, although this has not been consistent. Persistent infection (PI) with bovine virus diarrhea virus increases BRD occurrence, but it is unclear if PI calves affect other cattle in the feedlot. The complexity of BRD has made it difficult to define involvement of individual factors. Stressors may play a role as "necessary but not sufficient" components, requiring additive effects to cause disease.

Résumé — Épidémiologie complexe respiratoire bovin : Quelles sont les preuves de facteurs prédisposants? Le complexe respiratoire boin (CRB) est la maladie des bovins de boucherie la plus coûteuse en Amérique du Nord. Elle est multifactorielle, avec divers stresseurs physiques et physiologiques qui, une fois réunis, prédisposent le bétail à la pneumonie. Cependant, des efforts pour discerner les facteurs les plus importants n'ont souvent pas permis de fournir des réponses définitives. Les veaux sont le plus à risque peu de temps après le transport. Les facteurs de risque incluent l'achat directement à la ferme et l'amalgame. Il n'a pas été possible de déterminer si ces pratiques augmentent ou non la susceptibilité, rehaussent l'exposition ou représentent des facteurs associés à une mauvaise gestion. Les veaux d'un poids inférieur semblent être plus à risque, même si ce facteur n'est pas constant. L'infection persistante par le virus de la diarrhée virale bovine augmente l'occurrence du CRB, mais il n'a pas été possible de déterminer si les veaux avec une infection persistante affectent les autres bovins dans le parc d'engraissement. La complexité du CRB a compliqué la définition du rôle des facteurs individuels. Les stresseurs peuvent jouer un rôle en tant qu'éléments «nécessaires mais non suffisants», exigeant l'ajout d'autres facteurs pour le déclenchement de la maladie.

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Introduction

Bovine respiratory disease (BRD) is the most costly disease of beef cattle in North America (1). It is also one of the most extensively studied diseases, with research beginning in the late 1800s and continuing today. *Mannheimia haemolytica, Pasteurella multocida, Histophilus somni,* and *Mycoplasma bovis* are the bacterial agents that have been most consistently implicated in BRD. This causal association is based upon criteria that include isolation from clinical occurrences of BRD (2–6), vaccination trials (7–9), and serologic surveys (10,11). While *M. haemolytica* has traditionally been the most common bacterial isolate (12,13), an apparent increase in prevalence of other agents may suggest new emerging patterns of pathogens (2,4) or may simply be the result of increased effort to detect the agents (3).

Efforts have been made to identify the primary bacterial pathogen based upon gross necropsy and histopathological lesions (4,14). However, given a typical interval of several days to weeks between disease onset and death, it is uncertain how representative necropsy findings are of initiating agents. Others have suggested that a presumptive diagnosis of certain organisms may be possible antemortem. For example, animals infected with *M. bovis* are described as "chronically ill and fail to thrive… lack of weight gain and failure to respond to treatment" (3). Studies examining feedlot cattle with chronic, non-responsive

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respiratory disease corroborated this description although other organisms were also identified, alone or in combination with *M. bovis* (3,5). In contrast, cattle with *H. somni* show few distinguishing features unless other systems are affected (6). The importance of distinguishing between etiologic agents is questionable, as the clinical presentation and case management does not typically differ significantly regardless of the pathogen involved. This consideration, along with the frequency with which multiple species are isolated, has resulted in most researchers making no distinction among the various pathogens. Instead, clinical signs are relied upon for the diagnosis of undifferentiated BRD.

Occasionally viral agents may produce a clinical syndrome consistent with BRD in the absence of bacterial co-infection (15), but their involvement is generally considered as antecedent to, or concurrent with, bacterial infection (16). Experimentally, a syndrome resembling BRD can be induced with exposure to *M. haemolytica* following infection by bovine herpesvirus-1 (BHV-1) (17). Similar results were obtained with endobronchial instillation of bovine viral diarrhea virus (BVDV) followed 5 d later by *M. haemolytica* (18). Natural BRD outbreaks have also demonstrated these synergisms (19). Other viruses that are commonly implicated include bovine respiratory syncytial virus (BRSV) and parainfluenza 3 virus (PI3V) (4,16). Antigens to BRSV and PI3V were identified in over 50% of clinically diseased lungs in a study in Mexico (20), while BVDV was identified in naturally affected calves in numerous studies (3–5,13,19,21,22). Serological data has linked BRD outbreaks to BRSV (23,24), PI3V and BVDV (21), as well as multiple concurrent viral infections (25,26). Recent work suggests that bovine respiratory coronavirus may be related to BRD, although it has received considerably less attention than other viral agents (15,27–30).

Despite overwhelming evidence of the infectious nature of BRD, researchers are generally unable to replicate the most common clinical presentation through experimental exposure to bacteria or viruses alone (17). Additionally, the implicated bacterial species can readily be isolated from the upper respiratory tract of normal cattle (31,32). Therefore, BRD is a multifactorial syndrome, with various predisposing factors being necessary to induce disease. Commonly proposed predisposing factors ("stressors") include transportation, commingling with other cattle, dust, cold, sudden and extreme weather changes, dehydration, hypoxia, exposure to endotoxin, cold coupled with wetness, and acute metabolic disturbances (33,34). These are thought to alter the respiratory mucosa or hinder cattle's immune system, either directly or through the effects of endogenous agents such as cortisol, making the calf more susceptible to opportunistic infections. The intuitive nature of this concept is appealing, and it is widely accepted and repeated throughout the literature. However, relatively little epidemiologic investigation has been done to confirm or refute the importance of these factors, and studies done thus far have been inconclusive. The purpose of this review is to critically assess these investigations to identify which factors have been confirmed to be significant as well as to highlight equivocal findings and gaps in research relative to BRD. Principally epidemiologic studies are included, although a few experimental studies are referenced. A future article will examine the efficacy of efforts to reduce the severity and frequency of BRD (35).

Proposed predisposing factors

Viral infections

Viruses are believed to predispose to bacterial infection in 2 distinct ways. First, viral agents can cause direct damage to respiratory clearance mechanisms and lung parenchyma, facilitating translocation of bacteria from the upper respiratory tract and establishment of infection in compromised lung. Secondly, viral infection can interfere with the immune system's ability to respond to bacterial infection (26,36). Unique among the bovine respiratory viral agents is BVDV, in that intrauterine infection can result in cattle that are persistently infected (PI). Cattle that were PI were over-represented among cattle chronically ill or dying in feedlots (37). In a Canadian feedlot study (22), 61.5% (8 of 13) of PI calves died, whereas in a Kansas feedlot study (38) 25% (22 of 86) of PI cattle died within 60 d of arrival. These rates were presumably higher than for non-PI herdmates, but no statistical comparisons were reported for morbidity and mortality of PI versus non-PI cattle in either study. Persistently infected cattle also shed large quantities of the virus, increasing the risk of cohorts becoming infected and being at risk for BRD. This is potentially significant, since 30% or more of pens may contain a PI calf (22,38) and Loneragan et al (37) found that exposure to PI cattle increased risk of treatment for BRD. This conclusion was supported by Stevens et al (39), who showed short-term exposure (13 to 18 d) to PI calves increased morbidity. Neither study identified an increased mortality risk attributable to exposure to PI cattle. However, because of the relatively low incidence of mortality, a study using a greater number of cattle is required to have adequate power to detect a difference in mortality attributable to exposure (37).

Other reports examining the effects of PI calves have reached different conclusions. A controlled experiment found no effect of exposure to BVDV PI calves on morbidity, mortality, or performance (40). Similarly, 2 epidemiologic studies found there was no difference in morbidity between pens with PI calves versus pens with no PI calves (22,41). The different conclusions among these studies may, in part, be due to definition of exposure — Loneragan considered cattle as exposed if they were housed in pens containing PI cattle or in pens adjacent to those containing PI cattle. Others considered only calves in pens with PI cattle as exposed. Regardless, the prevalence of PI cattle is quite low [studies have estimated prevalence from $< 0.1\%$ to 0.4% (22,37,38,41,42)], and PI cattle likely do not account for, nor contribute to, the majority of BRD (22).

Environmental factors

Shipping

Transportation is the most universally accepted non-infectious risk factor for BRD and led to the layman's term "shipping fever." The segmented nature of cattle production in North America guarantees that virtually all beef calves will be transported at least once in their lifetime; therefore, most researchers have attempted to identify what component of transportation has the greatest effect on incidence of BRD. The distance and/or time in transit have been examined in various studies, with conflicting conclusions. A large survey found a positive association between distance transported and morbidity (43). This report must be viewed cautiously, however, given the biases and flaws inherent in self-reported surveys of this nature. Two epidemiologic studies reached opposite conclusions. Pinchak et al (44) found an association between disease and distance traveled. However, various confounders that may affect morbidity such as weight of calf and presence of bulls that required castration were not considered in this study (44). Ribble et al (45) found that the distance from point of purchase to destination had no effect on incidence of BRD. While time of year was the only confounder accounted for in their analysis, the consistent association between "shrink" (weight loss occurring during handling and marketing) and distance traveled was interpreted by the authors to suggest other confounders had minimal significance.

In an experimental study, calves transported 12 h had higher morbidity levels than those transported 24 h, whereas there was no difference between those transported 24 h and control calves that were fasted but not transported (46). The authors concluded that sorting, loading, and early transit are likely the most stressful components of transportation. This conclusion is supported by other studies (47,48). Another experimental trial found that calves transported < 150 miles (< 240 km) had less morbidity than those transported 150 to 200 miles (240 to 320 km) (49). Interestingly, this was not a linear relationship; calves hauled < 50 miles (< 80 km) had numerically higher (although not statistically significant) incidence of clinical BRD than those transported 100 to 150 miles (160 to 240 km). While these distances may have been too short to discern any impact of transport, another trial by the same researchers found no relationship between a much wider range of transported distances [ranging from < 50 to > 1000 miles (< 80 to > 1600 km)] and mortality (49).

Method of transport is another variable that has been considered as a possible contributor to BRD occurrence. It was suggested in a comparison of North American and Australian production systems that mode of transportation may account for differing rates of BRD. The Australian cattle industry relies heavily on trains which have more open ventilation, while the North American beef industry utilizes double deck tractor trailers with more complete enclosure (34). This theory was not supported in a 1982 study, wherein Canadian cattle were compared according to transport via truck or train (50). The potential effect of location of a calf within a transport trailer was examined in one study. It was theorized that proximity to exhaust may influence subsequent illness, but no difference attributable to location in the trailer compartment was found (51).

Dehydration is a frequent sequela to transportation and has been suggested as a mechanism by which transport impacts disease. Two studies found a positive correlation between shrinkage and transportation time (45,49); however, shrinkage was not correlated with BRD in either of these, nor 2 other studies (46,51). A positive association between shrink and BRD was demonstrated in 1 study (52); however, failure to account for several confounding factors precluded reaching a definitive conclusion. The most important confounder was that "preconditioned" calves had less shrink and less morbidity. Thus, it is unclear whether less disease was attributable to less shrink or to the preconditioning.

Weather

Weather has long been implicated in occurrence of BRD because the highest incidence is observed in the fall (53,54). Nevertheless, one cannot conclude that the predominating weather conditions at that time are the cause of increased BRD. Fall is the traditional time for marketing beef cattle in North America, resulting in more at-risk calves being congregated at marketing points at that time of year. A higher density of disease organisms, therefore, is likely present at sale barns, order buyer operations and feedlots. There is also the potential for more stress for the calves as crowding, commingling, and competition for feed and water are exacerbated.

Human factors have also been proposed to be involved in the seasonality of BRD. Specifically, high cattle traffic and long work hours lead to fatigue among stockyard and feedlot workers at this time of year. Additionally, potential delays in loading, unloading, transporting, and processing, as well as identifying and treating sick calves, could worsen disease occurrence (53). Nevertheless, a higher incidence of BRD was found in the fall in a bull performance center, which would not face the same human factors and logistical issues as feedlots (55).

Many authors have suggested that sudden and extreme changes in weather conditions, rather than simply cold or inclement weather, predispose cattle to BRD. Attempts to examine this hypothesis have been modestly successful in demonstrating such a link. Ribble et al found that BRD mortality peaked at approximately the same time as the largest decrease in mean daily ambient temperature (53). However, the annual differences seen in BRD occurrence did not correspond with annual variation in weather. In that 4-year study, 1 of the 2 years with greatest BRD risk had the most severe weather, while the other year with above-average BRD incidence had the mildest weather. Two other studies found opposite correlations between BRD and the maximum range in temperature within a 24-hour period; in the first, increased variation in ambient temperature corresponded with increased disease (56), whereas in the second study increased temperature variation correlated with a decrease in BRD (57). A cow-calf study found no clear trend between daily meteorological measurements and incidence of BRD (58). Recently, the relationship of a variety of temperature measurements (daily mean, minimum, and range) with morbidity and mortality was examined (59). These researchers found that minimum temperature had a higher correlation with BRD morbidity than did temperature range or mean. There was no relationship among climate variables and mortality. Interestingly, there was a zero day lag between minimum temperature and morbidity; that is, more calves were treated on cold days. If it is assumed that BRD has an incubation period, it would seem improbable that the infection would be immediately apparent. Instead, this finding may be attributable to signs of disease becoming more notable during severe weather rather than a true increased risk.

Other environmental variables that have been investigated include relative humidity (56), wind speed (59) and precipitation (57,59), none of which appear to influence disease occurrence. MacVean et al (56) also included the effect of dust in the feedlot on respiratory morbidity, and although they suggested that dust particles are associated with BRD, significant challenges in data collection and analysis were described. Airborne dust was collected and separated by particle size over a period of months in 2 consecutive years. These data were then plotted parallel to morbidity data, and subjectively assessed to determine temporal relationship. Based on visual appraisal, the authors determined that cattle on feed 16 to 30 d had the closest correlation between disease and presence of dust. Using regression analysis, it was determined that a 15-day lag time from peak exposure to peak disease yielded the closest correlation. The investigators ultimately concluded that particles between 2.0 to 3.3 μm in diameter impacted BRD incidence. This conclusion was the same for each of the 2 years; however, the magnitude of the relationship was different, such that the data from both years could not be combined into a single equation. Other variables believed to impact BRD occurrence (age, weight, and history or source of cattle) were not included in the analysis. Given the methodology of this study, it may be viewed as being more effective in identifying what particle size is most likely to affect respiratory disease rather than determining if a relationship exists between disease and dust in general. In contrast to the implications of the study above, a controlled experiment failed to identify an impact of dust on respiratory tract clearance of pathogens in a goat model (60). Two limitations of this study were that the dust used had an average size much larger than that found by the epidemiologic study to be associated with BRD, and the measured outcomes did not include treatment or morbidity.

Management factors

Source of animals: Ranch versus sale barn

While environmental factors may affect BRD incidence, it is more important to identify predisposing factors within the control of the producer. Study of these subjects, therefore, has received more attention, although the results are often no more conclusive. It has been repeatedly demonstrated that newly received cattle are at greatest risk for BRD (43,56,57,61) As a result, actions taken at or around the time of receiving have been scrutinized. Calves purchased through a sale barn are more at risk than those arriving directly from farm sources (62,63). This may result from greater exposure to pathogens as well as increased stress during multiple episodes of transit, marketing, commingling. A common recommendation, therefore, is to avoid purchasing sale barn cattle and preferably buy directly from the farm or ranch of origin (52,64).

Other factors commonly associated with sale barn calves, however, may be responsible for the increased risk, rather than the sale barn process itself. For example, BRD incidence increases when cattle from multiple sources are commingled (43). This most commonly results from buying calves from one or more sale barns and combining through an order buyer; however, commingling by other means also increases BRD risk. One example is introduction of new arrivals into a group over the course of several days to weeks, which increases BRD incidence compared to filling the pen in a shorter period of time (50,57,65). Hence, commingling, rather than sale barn exposure, may play the greater role in BRD incidence. This idea was supported in a study by Ribble et al (66), in which all calves were purchased through sale barns. However, some groups or pens of cattle came from fewer sources (more calves per farm) and therefore had less commingling, while other groups came from a larger number of farms, meaning there was more commingling. Incidence of BRD was higher in groups of calves put together from more sources than those created from fewer sources. Unfortunately, there was no opportunity to compare commingled versus non-commingled calves that had not gone through a sale barn.

Step et al (63) compared morbidity among ranch-direct calves, market calves, and commingled calves (calves from ranch and market, penned together after arrival). They found commingled steers to be intermediate in respiratory disease rates (higher than ranch, but lower than market). However, it was not reported if ranch calves had higher rates of illness due to commingling, or whether the higher rates in the commingled pens were strictly attributable to the increased disease among market calves.

Age and weight

Feedlot cattle are arbitrarily categorized as "calves" or "yearlings," usually based upon weight and phenotype at the time of entry. Yearling cattle are reported to have a lower incidence of morbidity and mortality (64,67), although no data were provided to support the claim. This assumption was considered a potential explanation for variations in morbidity from year to year (54); however, the relationship has not been uniformly apparent. Only 1 of the studies reviewed provided the actual age of animals, and it related to bulls in a test station rather than feedlot cattle (68). Townsend et al (68) found age to be associated with fever, a classification largely intended as a proxy for BRD. The youngest calf was 5 times more likely to be diagnosed with fever when compared to the oldest calf, wherein there was a difference of 100 d in age (68).

Several studies suggested that lighter-weight calves were at greater risk than heavier ones (11,43,62,69,70). Gummow and Mapham (62) dichotomized cattle based upon being above or below the mean weight of the group. It was determined that calves weighing less than the mean were 1.4 times more likely to develop BRD than those weighing more than the mean. Bateman et al (70) compared the average arrival weight of calves later classified as sick to that of calves remaining healthy, and found a 7-kg difference. Although this difference was statistically significant, it is clinically irrelevant (it reflected a difference of 3% of arrival weight, a value well within the expected variability of weight of calves within a lot). Interestingly, re-analysis of the data found that weight at entry was not predictive of BRD at a group level (71).

Sanderson et al (43) categorized calves as < 250 kg, between 250 and 318 kg, and > 318 kg in weight. Calves weighing > 318 kg were less likely to develop BRD than calves weighing

< 250 kg (relative risk of 0.18, $P < 0.00$). There was also a trend ($P = 0.09$) for mid-range calves to have fewer respiratory events than those in the lighter weight category (43). Other studies have contradicted these findings. In multivariate analysis, Thompson et al (72) found no difference in arrival weight among animals that did not suffer from BRD, those that developed subclinical BRD (never treated but had lung lesions at slaughter), and those that were treated for BRD. This study primarily utilized lighter weight calves, with a mean body weight of 233.4 kg at arrival; no weight range was reported, but cattle weighing between 150 and 300 kg were eligible for inclusion in the study. It is possible that this inclusion criterion skewed the study population toward high-risk calves, preventing adequate comparison to what would typically be considered yearling cattle. Indeed, age at entry was listed as ranging from 5 to 10 mo. In addition, since the study was conducted in South Africa, cattle and/or management factors may have been significantly different from those typical for North America. Therefore, conclusions may be less applicable to US and Canadian cattle industries, although other findings (percent morbidity, percent with lung lesions, reduction in average daily gain (ADG) attributable to morbidity and lung lesions) were consistent with those detected in North America.

Studies conducted at commercial US feedlots have also failed to find a relationship between arrival weight and BRD. The mean and standard deviation for arrival weight in one study was 335 ± 59 kg (57). These cattle could be considered as too heavy to demonstrate a weight effect, because most of the calves may have been old enough to be considered yearlings. This seems unlikely, however, since weights ranged from 217 to 530 kg; assuming the cattle were normally distributed across this weight range, such a range would seem large enough to identify weight-related effects. Another study found no difference in arrival weight between calves later treated for BRD compared with non-treated cattle. Interestingly, cattle with lung lesions identified at slaughter actually had heavier entry weights than those without lesions (73). It is possible that the lesions were present at entry and did not reflect disease incidence in the feedlot. While cattle with lesions had lower average daily gain in the feedlot (a finding consistent with active disease), the effect of pre-existing lesions on ADG is unknown. Finally, stocker calves from the southeastern US had an association between weight and BRD in some, but not all, groups of calves examined, with lighter calves having increased incidence of BRD (44).

Gender and covariates with gender

Gender has been investigated in relation to BRD, with, once again, conflicting results. In 2 studies analyzing disease from birth through feedlot, male calves were at higher risk for BRD than female calves (74,75). Two studies that examined only cattle after feedlot arrival also found that males were at a greater risk than females for developing respiratory disease (57,76). An Australian study found steers were at slightly higher mortality risk than heifers (59). This was reported as crude mortality and was thus not exclusive to BRD. While BRD was the greatest single risk factor for death, it is unclear what effect conditions unique to males (urolithiasis) may have had on crude mortality.

In contrast with these studies, Loneragan's retrospective study of records of over 21 million feedlot cattle found a higher incidence of BRD-associated mortality in heifers than in steers from 1997 to 1999. No difference was observed between genders, however, for cattle from 1994 to 1996 (54). In a 1988 Canadian study, heifers were also at a greater risk of fatal BRD compared with steers (9). Heifers, however, were purchased in smaller groups and combined over a longer period of time than were steers; a practice associated with increased BRD. Extended commingling, therefore, may account for the difference in respiratory disease mortality between genders in this study. Other studies found no difference in respiratory disease between males and females, although one survey found cattle in mixed-gender pens were at higher risk than those in either exclusively steer or exclusively heifer pens (43).

Numerous factors have been investigated in attempts to explain why one gender may be more commonly affected by BRD. The 3 feedlot studies that found males at greater risk all categorized calves either as heifers or steers with no mention of bulls (57,59,76); however, many calves arrive at the feedlot as bulls and must be castrated. This may explain at least part of the increased risk of BRD in steers, because calves castrated after purchase may be at increased risk of BRD compared with calves castrated prior to arrival (44,77). Increased morbidity in steers may also be partly attributable to the so-called "buller" syndrome, wherein a steer is repeatedly mounted and ridden by penmates. One study found "bullers" have an increased risk of BRD when compared with other steers (69), while another study did not find such an association (78). Riding behavior can also occur among heifers displaying estrus. To prevent risk of injury and decreased weight gain, melengesterol acetate (MGA, a synthetic progesterone) is frequently fed to heifers to inhibit cycling. It has been suggested that the anti-inflammatory effects of MGA may also reduce chronicity of respiratory disease, possibly resulting in disparity of disease between heifers and steers. However, morbidity and mortality were unaffected by MGA supplementation (79), and a subsequent study found that lesions were worse in MGA supplemented heifers following experimental challenge with *M. haemolytica* (80).

Castration and dehorning

As alluded to above, castration after arrival has been proposed as a risk factor for BRD. Like most other risk factors examined, the association has not been consistent. Several studies regarding castration did not analyze morbidity as an outcome of interest. Instead average daily gain (ADG), or plasma concentrations of acute phase proteins or cortisol were reported (44,81,82); therefore, any association between castration and BRD is merely by extrapolation. Nevertheless, delayed castration has repeatedly been found to reduce ADG (44,77,81–85), a result that was not influenced by analgesia during castration (84). This suggests that castration is a stressful event. Indeed, castration of large bulls increased plasma cortisol concentrations (81). Given the immunosuppressive nature of increased cortisol levels, castration of older bulls may put them at greater risk of BRD than non-castrated cattle or those castrated at a younger age. This supposition was supported by several studies (77,83,85), whereas others found no association or inconsistent findings between delayed castration and BRD (77,83,84). It is possible that failure to castrate at an early age is indicative of poor management in general, and the cumulative effects of poor management (rather than delayed castration) result in increased disease. Such a postulation would be difficult to assess.

Dehorning is similar to castration in that it is painful and is recommended to be performed early in life. Substantial research has been done on the immediate responses to dehorning, but few studies have evaluated longer term morbidity associated with this procedure. Martin et al (50) found increased BRD in groups where greater than 30% of the calves were dehorned. Others found inconsistent effect of age at dehorning on weight gain (86), although calves dehorned in the feedlot had lower average daily gain (87,88). This effect was accentuated if calves were castrated at the same time. However, BRD morbidity was not measured in any of these latter studies.

Regardless of the negative effects that may result from dehorning and castration, if calves arrive at the feedlot with horns and/or testicles the procedures should be performed to meet current industry standards. The only questions are how and when they should be performed. Most studies comparing castration methods examine surgical (knife) castration to banding. The trend has been for surgical technique to be preferred (77,82), with none of the reviewed studies identifying an advantage to banding. This statement concerns castration of older calves and yearlings, not pre-weaning castration. Studies examining young calves do not typically measure BRD and thus were not reviewed. One study compared 2 methods of surgical castration–emasculation versus ligation of the spermatic cord. No significant difference in morbidity was attributable to method (85). An advantage in ADG was found for castrating at arrival but no significant difference in morbidity was detected due to delaying the procedure 1 or 2 wk (85).

Other considerations

Impact of cattle characteristics

Disposition

A variety of other factors have been examined as to their relation to BRD. Fell et al (89) assembled 2 groups of cattle deemed "nervous" and "calm" based on behavioral scores under defined conditions. The study found that nervous calves were more likely to be treated for disease in the feedlot than were calm calves, although their assessment was not confined to BRD.

Genetics

Heritability of BRD susceptibility appears to be low (74,90), but breed differences have been detected. Braunvieh cattle appear to be the most susceptible, and animals of composite breeding have greatest resistance (74,90). Other studies have reported varied findings of breed and BRD susceptibility. A Swedish bull test study reported Angus and Hereford bulls to be at higher risk of disease compared with other breeds (24); however, the study was not designed to assess breed effects, and the authors cautioned about the validity of this finding. Another study also found Herefords to be at higher risk, but in contrast to Hagglund et al (24), Durham et al (23) found Angus to have decreased susceptibility compared with other breeds. An Australian study compared *Bos taurus* (represented by several breeds) with *Bos indicus* (represented by Santa Gertrudis and Santa Gertrudis cross) cattle for BRD incidence and found *Bos taurus* to be at greater risk for BRD than *Bos indicus* (59). Given the evolutionary origin of these types of cattle (*Bos indicus* being from hotter, drier climates), disease susceptibility could be expected to vary with geographic location and climate factors, and may not apply universally. As BRD resistance is poorly heritable, it may be expected that hybrid vigor is beneficial in reducing respiratory disease. This was confirmed in a study that found crossbred cattle had a lower incidence (90). Interestingly, a report published later by the same researchers found no benefits of heterosis among composite cattle compared with purebreds (91).

Parental factors may play a role in BRD occurrence. One study found that calves from younger dams had higher pre-weaning incidence of BRD but lower post-weaning BRD rates (74). Surprisingly, dams that appeared to be resistant to BRD were more likely to have calves that were susceptible (90). Both of these findings may relate to strong and persisting passive immunity preventing development of active immunity. Heifers have lower antibody levels in colostrum, thus their calves would be susceptible at a younger age. Cows with greater resistance would provide longer lasting passive immunity, possibly interfering with development of acquired immunity (90). The importance of maternal transfer of immune factors was further bolstered by a study that found vaccination of dams for BHV-1 and BVDV prior to calving decreased BRD in pre-weaned calves (92). Benefits of passive immunity appear to extend beyond weaning. Calves diagnosed with failure of passive transfer (assessed with plasma protein) continued to be at higher risk for respiratory disease even in the feedlot (75).

Conclusions

Bovine respiratory disease will continue to be an extremely costly condition. Although much research has been done regarding its determinants, there are only a few conclusive findings. Calves are clearly at highest risk shortly after transport/arrival. Consistent risk factors include being purchased from sale barns and commingling with cattle from multiple sources. It is unclear whether or not these practices increase susceptibility to disease, increase exposure, or are proxies for other poor management decisions. It seems likely that lighter-weight calves, which are presumably younger, are at greater risk for BRD than are larger cattle, although the association has not been consistent. Persistent infection with BVDV increases BRD occurrence, but it is unclear if the presence of PI calves has a major impact on other cattle in the feedlot. Other factors certainly impact development and prevention of BRD, but the complexity of the disease has made it difficult to define their role. These stressors may be "necessary, but not sufficient" components, thus requiring an additive effect to manifest as disease. Indeed, there may be numerous combinations of contributors that are "sufficient" to produce disease, with importance of an individual factor varying with presence of other variables. A number of challenges exist that make effective field research of BRD difficult [these are addressed in a future article (35)]; nonetheless, existing knowledge does not provide sufficient support for many assertions that have become dogma in discussing BRD. It is imperative that researchers and practitioners recognize the current limitations of knowledge and abilities, and to understand that much more remains to be done to control this expensive and persistent disease. CVJ

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