Prevention and Control of Bovine Respiratory Disease

R. Urban – Chmiel[1*], D. L. Grooms[2]

[1]University of Life Sciences, Lublin, Faculty of Veterinary Medicine, Institute of Biological Bases of Animal Diseases, SubDepartment of Veterinary Preventive, Akademicka 12, 20-033 Lublin, Poland
[2]Michigan State University, College of Veterinary Medicine, Department of Large Animal Clinical Sciences, MI USA.
***Corresponding author:** email: renata.urban@up.lublin.pl Tel.+48 81 445 60 36. Fax. +48 81 445 60 32.

Abstract

Bovine respiratory disease (BRD) constitutes one of the key health issues and most costly problems occurring in cattle in the U.S and all part of the world. Increased morbidity and mortality, decreased weight gains, decreased feed utilization, decrease carcass quality and increased prophylaxis and therapy lead to enormous economic losses. This is a disease complex that involves multiple microbial pathogens (viruses and bacteria), environmental and host predisposing risk factors. Increasing beef and dairy production in all part of the world will benefit from improved prevention and control of BRD. The use of management strategies, such as preconditioning programs, has a significant potential to decrease BRD cases and overall negative impact. Other programs, such as metaphylaxis, are useful in situations where calves entering a feedlot are at "high risk" for developing BRD. The cattle health industry should continue to identify means of BRD control though the development and use of new technologies with the aim of enhancing resistance, reducing risk factors and decreasing pathogen exposure.

Key words: Bovine respiratory disease, viruses, bacteria, metaphylaxis, vaccination

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Introduction

Bovine respiratory disease (BRD) constitutes one of the key health issues and most costly problems occurring in cattle in the U.S and all part of the world. This disease syndrome was originally termed "shipping fever" since signs often occur shortly after arrival in the feedlot. Buhman et al. (2000) reported that about 91 percent of calves diagnosed with BRD were diagnosed within the first 27 days after arrival. Some research (Edwards, 1996) has shown that morbidity risk of respiratory disease cases in feedlot cattle occur within the first 45 days after arrival to the feedlot and was highest in weeks 1 to 3, after that the morbidity decreased through the end of the 12-week period. Clinical signs most commonly observed include high fever (about 40-41.5^{o}C), depression, decreased appetite, nasal and ocular discharge, coughing and varying degrees of dyspnea. The etiology of BRD is almost always polymicrobial in nature and most generally is associated with predisposing environmental or host risk factors. Some of the pathogens involved in BRD may also be involved in other disease syndromes including gastroenteritis, arthritis, and encephalitis. The severity of disease is dependent on multiple factors including the predisposing risk factors, the microbial pathogens involved, and the management strategies used to control the problem (Bagley et al. 1997, Duff and Galyean, 2007).

Epidemiology and economic impact

Increased morbidity and mortality, decreased weight gains, decreased feed utilization, decrease carcass quality and increased prophylaxis and therapy lead to enormous economic losses. BRD accounts for approximately 75 percent of feedlot morbidity and 50-70 percent of all feedlot mortality (Edwards, 2010; Loneragan et al. 2001). The percent of morbidity and mortality depends on the management system in place, prevention program and the kind of pathogens involved. For example according to Duff and Galyean (2007), higher morbidty rates but fewer fatalities is typically observed when viral pathogens are primarily involved. In calves with bacterial infections only – there is sporadic morbidity, but higher mortality. The highest number of animals affected and higher mortality are observed in case of mixed viral and bacterial infections.

Annual losses to the US cattle industry are estimated to approach US$1 billion, whereas preventative and treatment costs are over US$3 billion annually (Griffin, 2006; Snowder et al. 2007). The average cost of a single treatment was estimated at US$15.60. This cost is amplified to US$92.30 when indirect costs are also considered such as reduction in average daily gain (ADG) and feed efficiney, and decreased carcass value (Schneider et al. 2009).

Diagnosis

Diagnosis of BRD can be done by different methods. Classical methods are based on physical examination and observation. Often observations are quantified in the form of a clinical score. The following clinical scoring system has been suggested by Perino and Apley (1998):

1- noticeable depression without apparent signs of weakness;
2- marked depression with moderate signs of weakness without significantly altered gait;
3- severe depression with signs of weakness such as significantly altered gait
4- moribund and unable to rise;

According to this scoring scale, calves with a rectal temperature higher than 40^{o}C and clinical score $\geq$1 need therapeutic treatment. Methods such as this are used commonly to consistently direct clinical treatment, but do not necessarily identify the causative pathogen.

The second diagnostic method is to use laboratory tests to identify microbial agents involved. Several samples can be taken to identify pathogens involved in BRD. These include blood, nasal or nasopharyngeal swabs, tracheobronchial lavage and tissue samples at necropsy. A firm understanding of the disease pathogenesis is necessary to select the correct sample and interpret the results. There are many useful laboratory methods available for identifying both viral and bacterial pathogens including culture, immunohistochemistry (IHC), antigen capture ELISA, culture and PCR assays (Duff and Galyean, 2007). We can also find some authors suggestion (DeRosa et al. 2000, Nikunen et al. 2007), that identification of ethiologic agents from sick calves can also be helpful in appropriate therapy and prevention of BRD. One useful method for identification of calves with predisposition to BRD after transportation is to identify changes in acute-phase proteins, including haptoglobin and fibrinogen. Some authors (Arthington et al. 2003, Svensson et al. 2007) suggest that changes in acute-phase proteins, such as haptoglobin, could be useful as a support in diagnostic of high risk calves after transportation.

Predisposing factors

Although in the majority of circumstances, BRD ultimately involves a microbial pathogen, there are multiple predisposing factors that work in synergism with the bacteria and viruses leading to clinical disease (Duff and Galyean, 2007, Callan and Garry, 2002). Predisposing factors may be related to the host or the environment. Host factors may include age, sex, breed, immune status, genetics and concurrent disease. Environmental factors include, but are not limited to, ambient temperature, humidity, ventilation, noxious gas concentrations and dust particles. The risk of BRD is often increased with management practices that increase stress. These practices include weaning, transportation, diet change, high stocking density, handling, and surgical procedures (dehorning, castration). Mixing of cattle leading to changes in social structures has been shown to be detrimental. As an example, mixing of steers and heifers increased risk for initial respiratory disease morbidity with an average Incidence Rate Ratio (IRR) of 3.7 times greater than non-mixed groups. Similarly, cattle from multiple sources (IRR = 2.0) and arriving from increased distance (IRR = 1.001) were also associated with increased initial respiratory risk (Sanderson et al. 2008).

Entry weight of calves at feedlot arrival may be associated with decreased morbidity risk. Sanderson et al. (2008) categorized calves as < 250 kg, between 250 and 318 kg, and > 318 kg in weight. Calves weighing over 318 kg were less likely to develop BRD compared to calves weighing below 250 kg (IRR-0.18, *P*, 0.00). Weight is likely an indicator variable for age in its relationship to morbidity risk. Younger calves are more susceptible to potential pathogens. These calves have less immunity and experience more stress in the transition to the feedlot and may respond less efficiently and fully to exposure to respiratory pathogens compared to older cattle.

One of the most important predisposing factors for BRD is transportation. Many variables can lead to increased stress and increased risk of BRD including loading and unloading, time duration of transport (Dixit, et al. 2001), food and water deprivation and the weather conditions. After arrival into a feedlot calves may be dehydrated, may show a decrease of appetite and in some of them we can observed an early stages of respiratory disease clinical signs. The current implemented of different technologies in beef cattle production in North America take that all calves will be transported during their lifetime and the time of feedlot. It's seems to necessary to identify which of the factors connected with transportation has the most critical in increasing of BRD incidence. For example weather conditions, kind of transportation and the distance or time of transit which have been examined in various studies, with different conclusions. For example Shake et al. (1980) suggested that calves transported below 240 km had less morbidity than those transported 240 to 320 km. The incidence of respiratory disease risk increase by 10% for each 160 km of transport distance.

Diets for newly received cattle should be formulated to adjust nutrient concentrations for low-feed intake and to provide optimal performance during arriving and acclimatization. Duff and Galyean (2007) confirmed the correlation between nutrition of stockers, immunoglobulin production and respiratory disease frequency. Low energy and protein concentration in feed increase suppression of immunological response and decrease of ADG in calves. According to Galyean et al. (1999) the concentration of chosen nutrients in feed during the first 4 week of feedlot should contains: 80 – 85% dry matter 20% - 26% protein and ≥60% or as say Taylor et al. (2010) 72% energetic substances.

Muggli-Cockett et al. (1992) suggest an important role in the incidence of BRD may be sex, observing that the incidence of BRD was greater in male calves than in female calves during both preweaning and feedlot periods. According to Snowder et al. (2005, 2007) breed differences may also have an influence on incidence of morbidity and mortality in calves. For example the highest incidence of BRD among feedlot calves was found in Braunvieh calves, but the highest mortality rates (18%) were observed in the Simmental. In the case of dairy breeds, the Friesian Holstein calves were significantly more susceptible for BRD in comparison to other breeds. The two most popular US breeds, Angus and Hereford, did not have higher incidences of postweaning BRD when compared to other feedlot breeds such as Charolais, Gelbvie, Limousin, Red Poll, Simmentaler or Belgian Blue, which are not as popular as the first one (Muggli-Cockett et al. 1992). According to these authors there is genetic correlation between increased birth weight and increased incidence of BRD during the pre-weaning and post-weaning periods. These differences in morbidity and mortality rates among breeds suggest a possible genetic diversity in immune responses among breeds. However the direct genetic effect on incidence of BRD is likely not large (Snowder et al. 2005).

Infectious agents

The agents responsible for BRD in cattle are both viral and bacterial. The viruses primarily involved in BRD include:
(i) IBR – BHV1- Infectious Bovine Rhinotracheitis Virus – Bovine Herpes Virus (BHV-1)
(ii) BVDV – Bovine Virus Diarrhea Virus
(iii) PI-3 – Parainfluenza 3
(iv) BRSV – Bovine Respiratory Syncytial Virus

The main role of these viruses is connected with establishing an environment that is favorable to colonization and replication by pathogenic bacteria resulting in pneumonia. Viruses may use different methods to accomplish this task. Viruses may cause alteration in mucosal surfaces such that adhesion of bacteria to virus-infected cells is enhanced; further colonization occurs more readily in areas of virus-induced mucosal erosion than in intact mucosa (Rivera-Rivas et al. 2009). Viruses can also cause modification of the innate and adaptive immune systems through altered alveolar macrophage function, suppression of lymphocyte proliferation and induced apoptosis, and modified cytokine and other inflammatory mediator release (Srikumaran et al. 2007). The bacteria commonly isolated from clinical BRD have been identified as *Mannheimia haemolytica* (formerly *Pasteurella haemolytica), Pasteurella multocida*, *Histophilus somni* (formally *Haemophilus somnus),* and *Mycoplasma bovis* (Autio et al. 2006, Frank et al. 2002, Rice et al. 2007). The viruses involved in BRD have been shown to work synergistically with these bacteria in creating more severe BRD. As an example of this synergism, primary viral infections can result in increased release of cytokines i.e. IL-1, 8, that activate and increase the migration of neutrophils and inflammatory process (Leite et al. 2002). This can result in greater adherence of bacteria, such as *M. haemolytica*, to bronchial epithelial cells, causing progressive inflammation characterized by fibrinous bronchopneumonia, the most acute form of BRD. We can say that between respiratory virus infections and *M. haemolytica* there is a synergic cooperation, which leads the colonization of these pathogens in lower respiratory tract (Hodgson et al. 2005).

BRD Control Programs

Implementing BRD prophylaxis and control systems benefit producers by reducing economic loss. It also benefits consumers because of the reduced disease incidence which has both food safety and quality implications. As with any disease control program, BRD control can best be accomplished by focusing on the following
(i) Increase in disease resistance by,

- Integrated vaccination programs against both viral and bacterial pathogens involved in BRD
- Sufficient nutrition program with good quality diet especially for calves exposed to stress conditions. The nutrition should be rich with energy, should contains high protein concentration and proper micro nutrient concentrations including minerals such as Zn, Cu, Fe and Se and vitamins E, B complex and C);

- Reducing stress brought on my management practices.

(ii) Decrease in exposure to BRD pathogens by,
- Reducing the risk of infected animals being introduced into a herd
- Bringing in only animals from uninfected herds
- Bringing in only animals from herds with a known effective vaccination program
- Avoiding the purchase of animals from sales barns
- Testing new animals for persistent infections
- Isolating new animals for 30 days before allowing contact with animals on-farm
- Sanitation to reduce pathogen build-up
- Isolation of sick animals.

Metaphylaxis

Mass treatment (mass medication) - administration of antibiotics especially long acting for control of bovine respiratory disease on arrival is appropriate for calves that may experience acute illness before generation of an effective immune response from a vaccination protocol, also known as “high risk” calves. The aim of metaphylaxis is to reduce the incidence of acute-onset BRD in highly stressed and newly received calves. In the case of “high risk” calves, for example unweaned, comingled, transported, non-vaccinated etc., antibiotic administration can be an effective means of BRD control. Using a post arrival metaphylactic program, we can observe a reduction of diseases by 50% and reduction of mortality by 25%. Metaphylaxis programs using specific antibiotic administration should be introduced only under the direction of a veterinarian. Using antibiotics increases the risk of developing resistance among bacterial strains, so it’s necessary to select and use chosen antibiotic carefully and avoid inappropriate uses. Only administration at the recommended time period, such as post transportation or post weaning, is appropriate. Some authors (Thomson and White, 2006) suggest that metaphylaxis can be used in conjunction with immunization program is beneficial for reducing BRD occurrence in newly received calves.

There are many antibiotics which are used in metaphylaxis in calves considered “high risk”. When considering metaphylaxis, it is necessary to know that not all antibiotics used in therapy have a beneficial effect in reducing BRD, therefore only approved antibiotics should be used. In the United States, those approved for metaphylaxis inlcude: tilmicosin, florfenicol, tulathromycin and ceftiofour. In a study in which calves received a single dose of the antimicrobial drugs (one for each groups) tilmicosin (10 mg/kg), oxytetracycline (30 mg/kg) or tulathromycin (2.5mg/kg) on arrival at the feedlot, the most beneficial effect was observed after tulathromycin administration. This positive effect was observed in the case of morbidity and mortality (about three times lower) (Booker et al. 2007, Schunicht et al. 2002). The authors suggest that even though tulathromycin is a more expensive antibiotic, the cost of the overall metaphylactic program is lower not only because of the beneficial effect in decreasing BRD cases, but also because of significant increase in average daily gain and feed efficiency. Similar result were observed after administration of tulathromycin or tilmicosin in mixed-breed beef bulls in experiment carried out by Nickell et al. (2008). The percent of morbidity was decreased about two-fold in the case of tulathromycin injection and the percent of mortality was 3.6% and 13.5% for tulathromycin and tilmicosin respectively. Earlier studies (Booker et al. 2007) have shown that administration of florfenicol (40mg/kg) in calves after transportation, especially in “high-risk” groups, significantly reduced (more than 35%) BRD incidences during the first 3 week of feeding. Economic benefits of using tilmicosin or florfenicol administration in calves after transportation are also connected with increasing of average daily weight of about 1.78 kg/day and 1.86kg/day respectively (Jim et al. 1999). Other authors (Nickell et al. 2008) also suggest that administration of chosen antibiotics such as tilmicosin or tulathromycin has a beneficial effect on average body weight, about 1.13kg/day and 1.12kg/day respectively in high risk calves after transportation. Studies have shown that using florfenicol metaphylactically decreases average costs of treatment from US$3.11per animal to US$15.72 per calf (Step et al. 2007) It should be noted that in all of the metaphylaxis studies reported here, the authors suggest that sufficient vaccination program before movement into the feedlot would make metaphylaxis unnecessary and uneconomical.

Vaccination

Vaccination against important pathogens involved in BRD is a useful tool to help reduce the risk of BRD occurring. In the United States, vaccines against the viral pathogens IBR, BVD, PI-3, BRSV and the bacterial pathogens *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somnus* are readily available. They are available in different combinations and with respect to the viral pathogens, they can be found in both killed and attenuated forms. Research has demonstrated that appropriate use of these vaccines can reduce the risk of BRD. Optimal vaccine response requires providing an efficacious vaccine to an immunocompetent animal. Immunity takes 1 to 3 weeks to develop, and may require multiple doses of vaccine to elicit protective immunity. Upon entering the feedlot, timing of the initial vaccination may vary if cattle experience transit time of more than 12 hours, it may be beneficial to allow 1 hour of rest for every 1 hour of transit before administering the vaccination and processing protocols (Edwards, 1996). A study conducted comparing on-arrival versus delayed (14 days) vaccination with a multivalent modified-live virus (MLV) vaccine showed improvement in daily body weight gain at day 0 to14 and day 0 to 42 in the delayed procedure (Richeson et al. 2005). Ideally, calves entering the feedlot would be vaccinated prior to entry. This is best accomplished as part of a preconditioning program. These value added calf programs addresses vaccination and management strategies that provide the calf an opportunity to build immunity during a time when stress and disease challenge is minimal.

Preconditioning programs

An important strategy used to decrease the incidence of BRD is the preventive health program commonly referred to as “preconditioning” which is a planned management program before shipment to the feedlot. In general, preconditioning programs ensure that the animals have been weaned for a predetermined amount of time (usually 30 to 45 days), vaccinated for various infectious agents (bacterial and viral vaccines), treated with anthelmintics, castrated, dehorned, and acclimated to feed bunks and water troughs prior to being shipped to feedlots (Duff and Galyean, 2007). Several studies have shown that the “preconditioned calf” that was weaned 30 - 45 days with proper vaccines and anthelmintic treatment are more valuable and will bring a higher price. In one study, preconditioned calves had 7.2% better feed efficacy, about US $29.50/per head lower medicine cost and a 3.1% lower mortality rate (Cravey, 1996) when compared to similar calves that had not been preconditioned. In the case of calves in a preconditioning system, owners receive a higher price for healthy calves (after vaccination program), and lower price for the high-risk calves without complete vaccination program (Macartney et al. 2003). Dhuyvetter et al. (2005) suggested that preconditioning in calves is economically feasible, and feedlots could afford to pay a US $14.00 per head premium for preconditioned animals. According to Roeber and Umberger (2002) suggested that the benefit of preconditioned animals is US$ 8.50 - $9.50/cwt (1 cwt – 45.5kg).

Various accines are used in preconiditoning program in the USA. In most cases, preconditioning vaccination programs minimally include immunization directed against BVDV, IBR, BRSV and PI-3. Vaccines directed against *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* may also be included. Ideally, these vaccines are given twice prior to shipment to the feedlot with completion of the two shot series occurring 2 weeks prior to shipment.

Future perspectives

Increasing beef and dairy production in all part of the world will benefit from improved prevention and control of BRD. In North America, the cattle industry uses the largest amount of animal health products, consuming 37% of the global supply. The animal health market for cattle products is second only to companion animal, with over $1 billion U.S. attributed to vaccines (Wilkinson, 2009). The cost of all losses due to BRD approaches US$1 billion per year and the average treatment cost is US$15.00 per cattle (Schneider et al. 2009). Because of these significant economic losses, it is necessary to develop strategies which will reduce the incidence and impact of BRD both in dairy and feedlot cattle. In the future, logical changes will include the development of better management and nutrition technology, and improved genetics. According to McVey (2009) very important information will be learned by continuing to investigate the pathogenesis of BRD in cattle. Areas of research that will help to improve the prevention and control of BRD include:

- Improved vaccines, vaccine formulation and administration strategies
- Understanding the genetic basis of disease resistance
- Understanding the role of inflammation in the pathogenesis of disease

Most importantly, further enhancement of BRD control will be accomplished by:

- Use of epidemiological concepts to manage BRD, especially as it relates to understanding the relationships between pathogens and predisposing factors
- Developing strategies to manage or reduce stress, especially associated with transportation, handling, feeding, and mixing of cattle
- Developing new antimicrobial therapies and theraputic strategies that not only provide clinical cures but also minimize selection of resistant organisms;
- Implementation of effective disease prevention strategies such as metaphylaxis and vaccination programs
- Development of diagnostic tools and methods necessary for early intervention
- Improving research to production system technical knowledge transfer.

Conclusions

BRD is the most important health issue in US feedlots. This is a disease complex that involves multiple microbial pathogens, and environmental and host predisposing risk factors. The use of management strategies, such as preconditioning programs, has a significant potential to decrease BRD cases and overall negative impact. Other programs, such as metaphylaxis, are useful in situations where calves entering a feedlot are at “high risk” for developing BRD. The cattle health industry should continue to identify means of BRD control though the development and use of new technologies with the aim of enhancing resistance, reducing risk factors and decreasing pathogen exposure. This will take a commitment on the part of the industry and government agencies to support ongoing BRD research.

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