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Article Review

Bovine Respiratory diseases in calves (BRD)

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ABSTRACT

Diseases of the bovine respiratory system are among the most common and significant illnesses affecting the cattle business worldwide. It is a multifactorial syndrome brought on by a confluence of environmental stressors, animal immunological response, and infectious organisms such as bacteria and viruses. For prevention and control efforts to be effective, BRD is necessary. These consist of appropriate immunization schedules, stress-reduction strategies, and early identification tactics.

INTRODUCTION

The prevention and management of BRD have received more attention in recent years because of its significant effects on the dairy and cattle industries' profitability and productivity. The illness frequently manifests soon after stressful situations like weaning, moving, or traveling, which weaken the immune system and provide an environment that is conducive to infections. The disease is primarily caused by primary viral agents like Bovine Herpesvirus-1 (BHV-1), Bovine Viral Diarrhea Virus (BVDV), and Bovine Respiratory Syncytial Virus (BRSV). Secondary bacterial infections like Mannheimia hemolytica, Pasteurella multocida, and Mycoplasma bovis frequently follow. The severity of lung lesions and clinical symptoms is influenced by these infections **(Bednarek et al. 2012, Chai et al. 2022, Brito et al. 2023) .**

A comprehensive strategy that includes appropriate immunization programs, stress management techniques, nutritional support, and prompt treatment interventions is necessary for effective BRD care. Furthermore, the investigation of other approaches such immunomodulators, probiotics, and phytogenic substances has been prompted by growing worries about antimicrobial resistance. In order to enable timely and precise therapy, ongoing research endeavors seek to better understand pathogen-host interactions and find early diagnostic markers. (**Andrews, 2004 and Donlon et al. 2023).**

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Review methodology:

This review attempts to give a thorough overview of publications published between 1914 and the present. It was done using Google and includes all relevant articles, regardless of the type of magazine or publisher. Includes the pathophysiology, clinical signs , diagnostic techniques, etiological variables, and current BRD treatment and prevention strategies. It helps to improve disease management procedures and raise the productivity and health of cattle by bringing attention to recent developments and difficulties. Calves, BRD, phagocytosis, Pco2, haptoglobin, fibrinogen, MDA, diagnosis, and treatment were all included in the search phrases.

Causes and development of BRD:

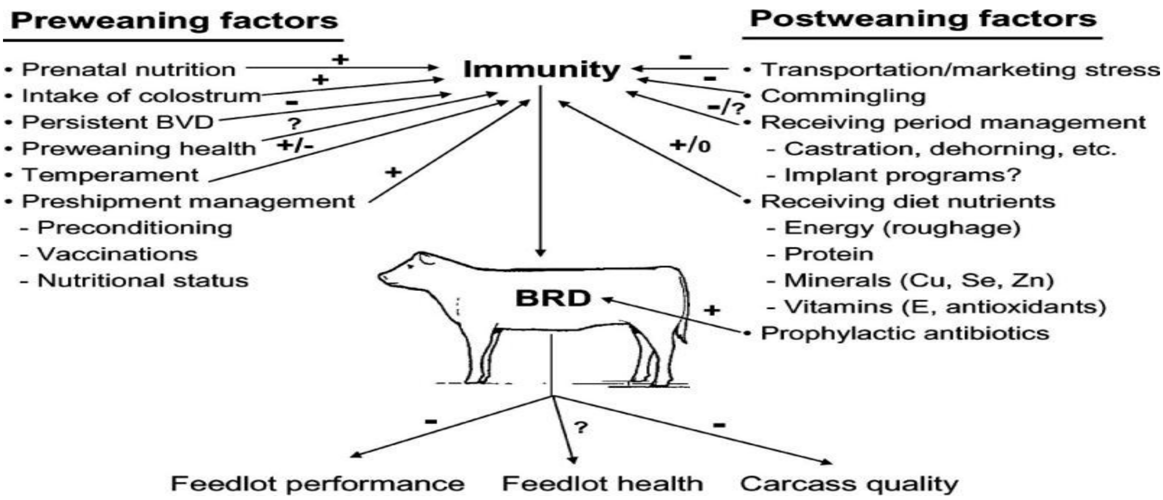
The causes of bovine respiratory disease (BRD) are complex and mostly include interactions between pathogenic pathogens and environmental stresses. The disorder is mostly caused by viral pathogens, including Parainfluenza-3 Virus (PI3V), Bovine Respiratory Syncytial Virus (BRSV), Bovine Viral Diarrhea Virus (BVDV), and Infectious Bovine Rhinotracheitis Virus (IBRV). By impairing the animal's immune system, these viruses open the door for more serious bacterial infections. The most commonly implicated bacteria are Mycoplasma bovis, Pasteurella multocida, Histophilus somni, and Mannheimia hemolytica. **(Robb et al. 2007 and Donlon et al. 2023)**.
The severity and stage of the infection affect the clinical manifestations of BRD. Fever, coughing, nasal discharge, elevated respiratory rate, lethargy, and decreased feed intake are typical symptoms **(Nutsch et al. 2005).**
Animals with severe pneumonia may exhibit symptoms like cyanosis, open-mouth breathing, and profuse salivation. Effective management and a decrease in death rates depend on early detection of these indicators **(Robb et al. 2007 and Duanghathai et al. 2022)**

Animals with a robust immune system are capable of effectively combating viral infections; however, cattle experiencing immune suppression due to stressful conditions can no longer fend off these viral agents, which then penetrate the respiratory tract and disrupt the protective barriers of the normal trachea and lungs. Once these defenses are compromised, bacterial agents can infect the respiratory system **(Powell, 1914).** The onset of Bovine Respiratory Disease (BRD) is triggered by environmental stressors and viral infections that diminish the lung's defense mechanisms, facilitating bacterial colonization. The mixing of cattle from various sources and significant fluctuations in environmental temperatures are primary factors that lead to disease outbreaks in feedlots **(Robb et al. 2007, Duanghathai et al. 2022).**

Table. Causes of BRD (Bagley , 1997)

Stress Factors	Viral Agents	Bacteria
Heat , Cold , Anxiety, Dust Nutritional deficiencies Irritant gases , Surgery Dampness, Injury , Fatigue Dehydration, Hunger	PI3, IBR , BVD, BRSV Adenovirus, Reovirus Rhinovirus, Enterovirus Herpesvirus IV , MCF	*Pasteurella haemolytica* Hemophilus Other

BRD is multifactorial:



Pre-and post-weaning factors affecting bovine respiratory disease (BRD) in beef calves and resulting outcomes of the disease (Lynch et al., 2010**)**.

Transporting cattle from various herds can introduce different bacterial and viral flora. This exposure usually happens alongside the stress related to shipping, which can include adverse weather conditions, alterations in feed and water sources, and moving to a new location. The combination of transportation, the stress factors involved, and the encounter with unfamiliar bacterial and viral pathogens raises the likelihood of respiratory diseases in cattle that have recently been shipped **(Robb et al. 2007 and Duanghathai et al. 2022).**

Clinical findings and Diagnosis of BRD :

The development of BRD typically begins with a viral infection that damages the respiratory epithelium and disrupts the mechanisms of mucociliary clearance. This situation facilitates the invasion and colonization of bacteria in the lower respiratory tract. The immune system of the host reacts to these pathogens, which often results in excessive inflammation and damage to lung tissue, worsening respiratory distress and hindering the exchange of oxygen. **(Assie et al. 2004, Snowder et al. 2005, and Chai et al. 2022).**

Accurate diagnosis of Bovine Respiratory Disease (BRD) necessitates both clinical assessment and laboratory analysis. Veterinarians often employ methods like nasal swabs for pathogen identification through PCR, serological assays, thoracic auscultation, radiographic imaging, and ultrasonography. Additionally, necropsy results can offer further understanding of the disease's severity and help in identifying the causative organisms.

Erythrogram:

Calves with diseases exhibited a notable reduction in RBC count, hemoglobin concentration, and packed cell volume in those affected by pneumonia **(El-Bealawy, 2003 and Faris et al. 2010).** Calves with respiratory illnesses demonstrated a significant decline in RBC count, hemoglobin concentration, and packed cell volume, with no significant changes observed in MCV, MCH, or MCHC **(Faris and Abd El-Hamied, 2007; El-Bealawy, 2003 and Ahmed and Abd El-Hamied, 2006).**

Leukogram:

Neutrophils serve as the initial line of cellular defense against pathogens, while lymphocytes play a crucial role in both cell-mediated and humoral immunity **(Paape et al. 2003 and Janeway et al. 2005).** Meanwhile, several research studies have investigated the function and distribution of neutrophils and lymphocytes **(Buckham et al. 2007 and Riondato et**

al. 2008) in both naturally occurring and experimentally induced cases of bovine respiratory disease (BRD) **(Coomber et al. 2001 and Sandbulte and Roth 2002).**

Biochemical Parameters in the Blood:

Bovine Respiratory Disease (BRD) in calves can be identified through biochemical blood tests conducted in a laboratory. Parameters like blood gases (pH, PCO2, PO2, tCO2, and HCO3) are crucial for providing insights into the diagnosis, treatment, and prognosis of diseases impacting the respiratory system and acid-base equilibrium **(Radostits et al. 2005).**

The hypoxia associated with pneumonia affects the blood's oxygen-carrying capacity, leading to alterations in the balance of blood gases (**Cambier et al. 2002**). There was a notable rise in PCO2 and HCO3 levels, accompanied by a significant drop in both pH and PO2 levels.

Proteinogram:

Serum protein electrophoresis is a laboratory method utilized to separate serum proteins based on their size and electrical charge, thereby enabling the identification and quantification of different protein fractions **(Ceron et al. 2010).** The protein profile of the affected animals prior to treatment indicated that the overall serum protein levels were not significantly different, while a notable decrease in albumin was observed when compared to the healthy control group. The protein electrophoresis results for the diseased calves before treatment showed substantial alterations, with increased levels of α-globulin and total γ-globulin **(Faris et al. 2010).**

When comparing sick animals to clinically healthy calves of the same age and breed, calves with chronic respiratory illnesses displayed significantly elevated total serum protein levels relative to healthy calves, whereas the sick calves exhibited a significant shift in the concentrations of most protein fractions, presenting significantly higher amounts of α1, β1, β2, and γ-globulins, and lower albumin levels than those found in healthy calves **(Tothova et al. 2012 and Csilla et al. 2013).**

The protein profile of the affected animals indicated that the total serum protein levels were not significantly altered, attributed to the rise in serum globulin levels as a reaction to respiratory infections **(El-Bealawy, 2003 and Faris and Abd El-El-Hamied, 2007).**

Inflammatory markers:

The impact of BRD extends beyond the respiratory system; it also influences whole-body energy and nitrogen metabolism by triggering the immune response. Most studies on metabolite alterations due to BRD have concentrated on acute phase proteins, particularly serum fibrinogen and, most notably, haptoglobin **(Baumann and Gauldie, 1994).**

The concentration of serum haptoglobin (Hp) has been proposed as a method for guiding management decisions, based on findings showing an association between Hp levels and the need for treatment in cattle with BRD. Hp is an acute-phase protein synthesized by the liver in response to cellular damage. By assessing Hp concentration upon arrival, producers could potentially identify which animals are likely to stay healthy **(Step et al. 2008).**

Circulating levels of acute-phase proteins, such as serum haptoglobin, rise in response to infection and inflammation in cattle **(Richeson et al. 2013).**

Calves with the disease exhibited a marked increase in serum haptoglobin compared to healthy calves, and their levels significantly dropped in all treated calves, especially in groups B and C by the 10th day post-treatment, where the markers' levels nearly equaled those of the healthy calves **(Eleiwa et al. 2014).**

Oxidative status:

Reduced antioxidant capacity, along with heightened oxidative stress markers, significantly contributes to the development of the syndrome within the initial three weeks post-transport **(Chirase et al. 2004).** Oxidative stress is believed to be a crucial factor in the onset of various lung diseases, not only due to direct damaging effects but also through its role in the molecular pathways that govern lung inflammation **(Macnee, 2001).** Calves with disease exhibited a marked increase in the average serum MDA levels when compared to healthy calves **(Eleiwa et al. 2014).**

Immunity:

A- Changes in Immunoglobins:

Newborn heifers that experienced a failure of passive transfer of colostral immunoglobulins faced a higher risk of developing BRD compared to those that received sufficient colostral antibodies **(Van Der Fels-Klerxi et al. 2002)**.

Blood samples were obtained 24 hours after birth to assess plasma protein and serum immunoglobulin (IgG) levels. Respiratory illness in feedlot calves was linked to lower plasma protein levels, though serum IgG levels were not affected at 24 hours postpartum. Calves with insufficient plasma proteins at 24 hours after birth were at a greater risk of illness and respiratory conditions in the feedlot in contrast to those with adequate plasma proteins. These findings indicate that beef cattle producers should effectively manage both cows and calves to ensure successful passive transfer **(Godden, 2008; Ackermann et al. 2010; Berman et al. 2022).**

B-Changes in cellular immunity:

The presence of viruses within the bovine respiratory tract may modify the microenvironment of mucosal surfaces and the structure of bacteria, resulting in impaired mucociliary function and damage to cilia. Furthermore, viral infections may lower the levels of antimicrobial peptides, affecting bacterial adherence and invasion by modifying the host immune response. Diseased calves suffering from BRD prior to treatment showed a notable reduction in both the percentage of phagocytosis and the phagocytic index, whereas treatment with flumethasone led to a significant decline in cellular immunity on the 3rd and 7th days following treatment. In contrast, treating the calves with meloxicam did not affect any measures of cellular immunity, as reported by **Faris et al. (2010).** Diseased calves exhibited a significant rise in phagocytic activity (%) and the phagocytic index when compared to healthy calves. Calves treated with oxytetracycline (20 mg/kg bwt twice with a 48-hour interval) and Floxon (0.5 ml/10kg bwt) showed a significant decrease in both phagocytic activity (%) and the phagocytic index on the 3rd and 10th days post -treatment, while calves in the group receiving 5 mg/kg bwt daily revealed no significant changes when compared to diseased calves prior to treatment, as stated by **Eleiwa et al. (2014).**

Treatment of BRD:

The treatment of bovine respiratory disease (BRD) often includes antibiotics to address bacterial infections, along with anti-inflammatory drugs and supportive care measures like fluid therapy and nutritional assistance. Nevertheless, due to increasing worries about antibiotic resistance, management strategies that integrate multiple approaches are being prioritized. These strategies comprise effective vaccination programs against viral and bacterial pathogens, stress reduction through improved management and housing conditions, and the incorporation of immunostimulants, probiotics, and phytogenics as supplementary measures. It is generally more effective to administer antibiotics or sulfa medications via drinking water instead of feed, as sick cattle tend to stop eating but usually continue to drink water for a longer period **(Bagley, 1997).**

A variety of approved antimicrobials are available for managing respiratory disease by treating entire groups of cattle, including tilmicosin (Micotil®, Elanco Animal Health), oxytetracycline (Tetradure®, Merial), ceftiofur crystalline free acid (Excede™, Pfizer Animal Health), florfenicol (Nuflor®, Schering-Plough Animal Health Corporation), and tulathromycin (Draxxin®, Pfizer Animal Health) **(Robb et al. 2007).**

Several macrolide antibiotics, such as erythromycin, tylosin, tilmicosin, spiramycin, and tulathromycin, are authorized for the treatment and/or prevention of BRD in cattle **(Zhanel et al. 2001).** Although these antibiotics are typically well absorbed and attain effective levels in lung tissue, many of them have a high affinity for plasma proteins, limiting their distribution outside the blood vessels **(Jain and Danziger, 2004; Huang et al. 2010).**

Various studies have highlighted the positive impact of nonsteroidal anti-inflammatory drugs (NSAIDs), like meloxicam, in treating BRD. This disease is economically significant, particularly in the beef feedlot sector, and a crucial aspect of the disease's pathogenesis is the harmful cycle initiated by chemotaxis and the ensuing release of lysosomal substances from neutrophils. Other inflammatory mediators contribute to the inflammatory response, causing vascular changes in the lungs and leading to fibrin deposition on the lung and pleural surfaces **(Bednarek et al., 1999; Francoz et al. 2012)**.

CONCLUSION

It could be* concluded *that:

Bovine Respiratory Disease continues to pose a major risk to the cattle industry, characterized by its complicated causes and considerable financial implications. Addressing BRD calls for a comprehensive strategy that includes prevention, swift diagnosis, and timely treatment. Continued research is critical for discovering new treatment alternatives and enhancing disease management techniques, ultimately supporting improved animal health and production efficiency.

Respiratory illnesses impacted the hematological profile and caused alterations in both total and differential leukocyte counts. Additionally, they caused significant disruptions in blood gases, indicating respiratory acidosis, as well as changes in protein electrophoresis, various inflammatory markers, oxidative status, and finally, immunological parameters.
The use of draxxin combined with meloxicam in calves affected by BRD proved to be more effective than administering the antibiotic alone.

The combination of levamisole and draxxin improves both humoral and cellular immunity in calves affected by BRD.

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