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Review Article

Pathogens Associated with Bovine Respiratory Disease in Pre-weaned Cattle Calves – A Review

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Abstract

Bovine respiratory disease (BRD) is a multifactorial disease complex caused by factors including stress, primary viral infection and a concurrent bacterial infection. Stress includes environmental and managemental factors especially inadequate ventilation, comingling of calves, over-crowding and poor nutrition. Exposure to different kinds of pathogens like bovine herpes virus 1 (BHV-1), bovine viral diarrhea virus (BVDV), bovine respiratory syncytial virus (BRSV), bovine coronavirus (BoCV), infectious bovine rhinotracheitis (IBR), Mycoplasma bovis, Mannhaemia haemolytica, Pasteurella multocida and Histophilus somni causes BRD in immunocompromised cattle calves. Failures of transfer of passive immunity in calves predispose them to secondary bacterial infection. Immunohistochemistry (IHC) and molecular diagnostic tests like PCR with histopathological examination is more in use as compared to the traditional viral isolation and bacterial culture. Often thoracic auscultation and ultrasonography are employed for the primal BRD diagnosis in pre-weaned calves. This article deals with the various viral and bacterial pathogens associated with BRD.

Keywords: Bacterial and Viral Pathogen, Bovine Respiratory Disease, Bronchopneumonia, Immunocompromised Cattle Calves, Immunity

Introduction

Bovine respiratory disease (BRD) is the most common disease affecting cattle (Griffin, 1997) in the world. BRD is caused by a range of factors either solely or by their amalgamation. These factors include stress, primary viral infection and concurrent bacterial infection. This disease is a complex which causes pneumonia in calves (Lillie, 1974).

BRD being a multifactorial disease is engendered by exposure to different kinds of pathogens like bovine herpes virus 1 (BHV-1), bovine viral diarrhea virus (BVDV), bovine respiratory syncytial virus (BRSV), bovine coronavirus (BoCV), infectious bovine rhinotracheitis (IBR), *Mycoplasma bovis* (Stokka, 2010), *Mannhaemia haemolytica, Pasteurella multocida, and Histophilus somni* (Confer, 2009).

The immunocompromised status of a pre-weaned cattle calf due to stress and its subjugation by immunosuppressive viruses like BVDV, BHV-1, and IBRV makes it more susceptible to secondary respiratory infection by bacteria which are initially commensal of the respiratory tract (Edwards, 2010). But, now a days; new pathogenic patterns and increased pervasiveness of unconventional microbes in BRD is an event of consternation. The repeated isolation of multiple pathogens from BRD infected pre-weaned calves and the undifferentiated clinical signs seem to be a colossal comprehension gap with respect to this complex disease. The inability to replicate the clinical illustration via experimental exposure to bacteria or virus alone makes the question even more significant (Taylor *et al.*, 2010). The commensal similitude among different bacteria causing BRD in pre-weaned calves makes the conclusive diagnosis more dubious on the basis of general sign and symptoms (Griffin *et al.*, 2010).

Approach to older animals, lofty relative humidity, destitute quality of air, expanded stock density, dense and poor quality bedding and housing in close proximity of sick animals are major risk factors associated with BRD in cattle calves (Gorden and Plummer, 2010). Deficiency of trace minerals like Copper, Selenium, Zinc, Sulfur and handling stress are a few more attributing causes of BRD. Unanticipated dietary changes and commingling of divergent groups also predispose calves to BRD (Stokka, 2010).

The preeminent clinical signs correlated with BRD in pre-weaned cattle calves are abnormal breathing pattern like dyspnea and tachypnea, anorexia, sluggishness, increased rectal temperature and anomalous lung sound like crackles and wheezes (Buczinski *et al.*, 2014). Studies show that the incidence rate of BRD in calves of 12 weeks of age is more than the incidence rate in calves of 16 weeks of age and the extortionate incidence rate is in the first week of age. The incidence risk of BRD dwindles up to the age of 9 weeks but expands slightly after that for few more weeks (Schaffer *et al.*, 2016).

Diagnosis of BRD in pre-weaned cattle calves is not only important for the evaluation of disease risk and herd health but also it is of principal importance for assessing the latent operations contributing to the disease in the drove in a convenient way. Portrayal of flock problem via ante-mortem testing always depends on animal assortment. For latest picture of disease, animals selected should be in primitive stages of disease prior to treatment. With certain invasive techniques like tracheal wash and bronchoalveolar lavage, few indubitable non-invasive techniques like nasopharyngeal and nasal swabs are also used for the tryout of BRD in pre-weaned cattle calves. Immunohistochemistry tests (IHC) and molecular diagnostics like PCR tests with histopathological examination and other laboratory test like micro array analysis are now a days more in use as compared to the traditional viral isolation and bacterial culture. Serologic elucidations are a bit more complex due to the action plans of vaccination and the chronology of the sample collection (Cooper and Brodersen, 2010). Often thoracic auscultation and ultrasonography are employed for the primal BRD diagnosis in pre-weaned cattle calves (Buczinski *et al.*, 2014). Most of the laboratory tests explored above are although reliable but are inclined towards false positivity. Consequently, a handful of scoring systems like The California (CA) and Wisconsin (WI) clinical scoring systems may be found user-friendly to discern the BRD burden in pre-weaned dairy calves (Love *et al.*, 2016).

Morbidity and mortality due to BRD in cattle calves depend on the managemental factors, type of associated pathogen and prevention programme. In case of severe outbreaks, morbidity may reach upto 100% and mortality ranges from 4% to 20% (Joshi *et al*., 2016). Comparatively higher morbidity and lower mortality is observed in viral infections and sporadic morbidity with higher mortality is observed in bacterial infections. Maximum morbidity and mortality is observed in mixed infections (Duff and Galyean, 2007). In developing countries like India, the overall prevalence of BRD in cattle calves is 2.07%. Age-related susceptibility causes highest prevalence

of BRD (11.58%) in 0–1 month's age group calves. Environmental stress causes highest prevalence (3.61%) of BRD in cattle calves during winter season. Prevalence of BRD is higher in case of male calves (3.08%) as compared to female calves (Joshi, 2015).

Pre-weaned calf mortality depiction due to BRD is the selfsame from past twenty years. Control practices for respiratory diseases in calves cover weighty nutrition, bonafide vaccination, requisite ventilation in housing, vigorous immunity expansion via ample colostrum availability and substantial biosecurity practices (Gorden and Plummer, 2010). Efficient cold stress management also assist in controlling BRD in pre-weaned cattle calves.

Differences between BRD, Shipping Fever and Enzootic Pneumonia

Enzootic Pneumonia

Enzootic pneumonia is commonly an infectious respiratory disease in calves. Sometimes it is also called as viral pneumonia of calves but is not preferred based on the current understanding of etiology and pathogenesis. Enzootic pneumonia is mainly seen in calves less than 6 months old and its peak occurrence is from 2–10 weeks, but it can be observed in calves up to 1 year of age. It is more frequent in dairy than in beef calves and is seen mainly in veal calves and in housed dairy calves than in those raised outside in hutches. Peak incidence of disease generally matches with decline of passively acquired immunity by colostrum (Campbell, n.d.).

The etiology is similar to that for BRD complex in general. The pathogenesis includes environmental and management stressors and generally an initial respiratory viral infection followed by a secondary bacterial infection of the lower respiratory tract. Stress includes environmental and management factors especially inadequate ventilation, mixing of calves, over-crowding, and poor nutrition. Host related factors include partial or complete failure of passive transfer of maternal antibodies (Campbell, n.d.).

Shipping Fever

Shipping fever pneumonia also called as undifferentiated fever, is a multifactorial respiratory disease mainly caused by *Mannheimia haemolytica* and, less commonly by *Pasteurella multocida* or *Histophilus somni.* Shipping fever pneumonia is the outcome of assembling large groups of calves in the feedlots from different geographic, nutritional, and genetic backgrounds. The disease is seen at its peak within 7–10 days after assembly in a feedlot (Campbell, n.d.).

The pathogenesis of shipping fever pneumonia rotates around stress factors like weaning, exhaustion due to transportation over long distance, starvation, dehydration, chilling, commingling in auction markets, sudden nutritional change, dusty environment, etc. Concurrent viral infections cause suppression of host immune system, which allows the proliferation of commensal bacteria in the upper respiratory tract. Later, these bacteria colonize the lower respiratory tract and cause a bronchopneumonia in the cranioventral lung sections (Campbell, n.d.).

Common Bacterial Pathogens Associated with BRD

Mycoplasma bovis

M. bovis is a common commensal microbe present in the upper respiratory tract (URT) of cattle. Maintenance of *M. bovis* within a herd is attributed to its capability to cause chronic asymptomatic infection and its intermittent shedding. Ingestion of *M. bovis* infected milk is an important mean of its transmission in young calves. This microbe can be transmitted via aerosols, nose-to-nose contact, via feed, water, housing or other fomites (Caswell and Archambault, 1996).

Some studies show an association between bovine viral diarrhea virus infection, *Mannhemia haemolytica* infection and *M. bovis* infection due to their simultaneous isolation in various cases. *M. bovis*-associated pneumonia with co-infection by other bacteria accompanied by otitis media caused by *M. bovis* is very common (Caswell and Archambault, 1996).

Various factors important in pathogenesis of *M. bovis* are adherence to respiratory epithelium, antigenic variation,

invasion, immunomodulation, biofilm formation, and production of toxic metabolites. The membrane proteins of *M. bovis* help in the adherence to mucosal surfaces. Variable surface lipoproteins (VSPs) present with *M. bovis* exhibit extensive strain variation in their coding sequences. These VSPs convey *M. bovis* a huge capacity for antigenic variation and give a challenge for vaccine development against *M. bovis*. Several other factors enhancing pathogenesis of *M. bovis* are its products such as phospholipases, hydrogen peroxide, and superoxide radicals, which damage the respiratory epithelium of the host. The capability of *M. bovis* to make biofilms imparts it an increased resistance to desiccation and heat stress (Caswell and Archambault, 1996).

Failure of transfer of passive immunity in calves predisposes them for *M. bovis* infection. Innate immune responses like the alveolar macrophages are of supreme importance in the early removal of mycoplasma from the lungs. *M. bovis* infection cause strong inflammatory responses due to excessive TNF-a production by alveolar macrophages. Excessive neutrophil recruitment by macrophages and concomitant release of large amounts of inflammatory mediators cause severe mycoplasma disease. Ineffective adaptive immune responses cause chronic *Mycoplasma* infection. Variation of surface antigens mediates lesser clearance of *Mycoplasma* mediated by adaptive responses of host. Humoral immune responses including IgG play an important role in protection from *M. bovis*. *Mycoplasma* respiratory infection related immune-pathological components are mainly the large accumulation of lymphocytes in infected tissues, the secretion of pro-inflammatory cytokines, and extensive lung inflammation. Studies had showed that M. bovis promotes a mixed Th1-Th2 cytokine response (Caswell and Archambault, 1996).

M. bovis-associated pneumonia related clinical signs are although non-specific but sometimes otitis media, arthritis or both occur in the same animal simultaneously. This condition happens in beef cattle several weeks after the entry in feedlot. Clinical signs like head shaking, head tilt and scratching, rubbing of ears, ear droop, ptosis, nystagmus, circling and falling are due to ear pain and cranial nerve VII defects. Clinical signs related to *Mycoplasma* arthritis are similar to septic arthritis, which includes non-weight bearing lameness, joint swelling, and pain (Caswell and Archambault, 1996).

The low sensitivity and specificity of the available tests, subclinical infections and intermittent shedding of *Mycoplasma* make its diagnosis more dubious and delayed. Antibody titer does not show the clear picture of disease in the herd sometimes due to interference by the maternal antibodies present in colostrum. Isolation of *Mycoplasma* and confirmation can be done by antibody-based tests like immunofluorescence or immunoperoxidase test or preferably by polymerase chain reaction (PCR). Trans-tracheal wash is preferred over the URT samples for the diagnosis of *M. bovis* pneumonia in the live animal. Joint or tendon sheath aspirates can also be used for *M. bovis* detection in affected animals. Due to cell-surface associative nature of Mycoplasma, vigorously rubbed swabs should be taken for sampling. On the basis of histopathology and other findings, *M. bovis* presence in the samples can be correlated with the other associated pathogens. Lesions associated with *M. bovis* contains multiple necrotic foci filled with dry yellow to white caseous material causing fibrinous and caseonecrotic bronchopneumonia. *M. bovis* pneumonia is seen as subacute to chronic bronchopneumonia that can be suppurative and necrotizing (Caswell and Archambault, 1996).

Pasteurella multocida

P. multocida serogroup A is a commonly isolated gram-negative pathogen from both enzootic calf pneumonia cases in young dairy calves and shipping fever cases in weaned and stressed beef cattle in bovine respiratory disease (BRD). The concurrent viral infections and various other stress factors like shipping, co-mingling and overcrowding predispose the animals for *P. multocida* infection. Acute to subacute suppurative bronchopneumonia also called as lobular bronchopneumonia is seen in the cranioventral lungs that most often is not associated with pleuritic lesions. *P. multocida* possesses multiple virulence factors like adherence and colonization factors, iron-regulated and acquisition proteins, extracellular enzymes such as neuraminidase, lipopolysaccharide, polysaccharide capsule and a variety of outer membrane proteins (OMPs) (Dabo *et al.*, 2007). The adhesins, the polysaccharide capsule and the associated PLS are responsible for the colonization of bacteria, its escape from the host immune system, host tissue destruction and related inflammatory responses. Adhesins include type IV fimbriae, OmpA, neuraminidase and filamentous hemagglutinin (FHA). OmpA and various iron-binding proteins like hemoglobin-binding protein A, transferrin-binding protein A and bind fibronectin helps the bacteria in tissue invasion. The antiphagocytic properties of the bacterial capsule helps it in evading the host defense. The LPS factors of *P. multocida* are helpful in stimulating the inflammatory cytokines and causing pulmonary inflammation (Panciera and Confer, 2010).

Mannheimia haemolytica

Mannheimia haemolytica is predominant opportunist commensal bacterial pathogen of the nasopharynx related to BRD in feedlot cattle and especially in enzootic pneumonia in neonatal calves (Rice *et al.*, 2007). The important factors responsible for the pathogenesis and virulence of *Mannheimia haemolytica* are protein adhesins, capsular polysaccharide, lipopolysaccharide (LPS), iron-binding proteins, secreted enzymes and a ruminant-specific RTX toxin called as leukotoxin (LKT) (Panciera and Confer, 2010). The characteristic fibrinous bronchopneumonia also called as lobar bronchopneumonia caused by *Mannheimia haemolytica* is associated with leukotoxin-mediated infiltration and destruction of neutrophils and other leukocytes impairing the bacterial clearance. The synergism of LPS with leukotoxin complicates the situation by increasing the endotoxic activity (Rice *et al.*, 2007). The attachment of the bacteria to the tracheal epithelial cells is attributed by specific adhesins including a glycoprotein called as N-acetyl-D-glucosamine which also causes the oxidative lysis of the host neutrophils. The outer membrane components of the bacteria like protein A (OmpA) and the surface lipo-protein 1 helps in binding to the bronchial epithelial cells. *Mannheimia haemolytica* capsule also works as an adhesin. Factors like Neuraminidase and sialoglycoprotease alter the cell surface and help in bacterial adhesion to the host epithelial cells. The LPS factor bears endotoxic and proinflammatory powers to enhance the virulence of the bacteria. LKT causes alterations in the bovine leukocytes by promoting osmotic swelling, pore formation, apoptosis and also responsible for the release of proinflammatory cytokines, oxygen-free radicals and cellular protease (Panciera and Confer, 2010). Hence, targeted approach with the help of modern vaccines using culture supernatant containing leukotoxin and other soluble antigens alone or combined with bacterin is more helpful in preventing the *Mannheimia haemolytica* infection in the herds. The amalgamation of more differential diagnosis, more efficacious vaccines and therapeutic interventions along with improved managemental practices are the key tools for the effective control of *M. haemolytica* pneumonia in the animal populations (Rice *et al.*, 2007).

Histophilus somni

Various pathogenicity related factors associated with *Histophilus somni* which is a non-capsulated bacterium are the lipo-oligosaccharide (LOS) and the outer membrane proteins like transferrin-binding proteins and immunoglobulin-binding proteins (IgBPs). LOS help in the apoptosis of endothelial cell and are responsible for the evasion of bacteria from the host immune system by antigenic phase variations. LOS also causes thrombosis, inflammation and tissue destruction and assists the bacterium to evade host defenses. The surface-exposed fibrillar proteins called as IgBPs helps the bacteria to escape from the host immune system by binding with the Fc domain host IgG2 and making the bacteria resistant to phagocytosis and complement-mediated lysis. The histamine yielded by the bacteria also add strength to its virulence (Panciera and Confer, 2010).

Arcanobacterium pyogenes

The main virulence factor of *Arcanobacterium pyogenes* is a collagen-binding protein (CbpA) which helps the bacteria to bind it to collagen promoting its adhesion to the host cells. *Arcanobacterium pyogenes* also secretes a cholesterol-dependent cytolysin called as pyolysin which help as a pore-forming factor in the host immune cells. Type-II fimbriae and neuraminidases are also important bacterial factors which promote the adhesion of the bacteria to the host epithelial cells. The extracellular matrix-binding proteins called as fibronectins and the exoenzymes (DNase and proteases) secreted by the bacteria helps in tissue invasion and degradation of proteins and nucleic acids of the host cells. The property of *Arcanobacterium pyogenes* to make biofilm is a responsible factor for survival of the bacteria in the host immune cells especially in the macrophages (Panciera and Confer, 2010).

Bibersteinia trehalosi

The virulence factors of *Bibersteinia trehalosi* are pretty much similar to that of *Mannheimia haemolytica*. The main virulence factors include the bacterial capsule, LKT and fibrinogen-binding proteins. OmpA molecules are responsible for the adhesion of the bacteria to the respiratory epithelial surfaces of the host (Panciera and Confer, 2010).

Common Viral Pathogens Associated with BRD

Bovine Respiratory Syncytial Virus

Bovine respiratory syncytial virus (BRSV) is an important pathogen related to enzootic pneumonia in young dairy calves and summer pneumonia in nursing beef calves. BRSV is a Paramyxovirus from subfamily Pneumovirinae, and genus *Pneumovirus* which is a single-stranded, negative-sense RNA virus. BRSV plays an important role in bovine respiratory disease complex by predisposing the calves to secondary bacterial infections by *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* (Sacco *et al.*, 2014).

Calves less than 6 months of age are comparatively more susceptible to BRSV infection even in the presence of maternal antibodies provided by colostrum. BRSV transmission generally occurs via aerosol droplets from or direct contact with infected animals. BRSV infection in the calves is most commonly seen in the fall and winter months in temperate environment. Stress factors like weaning, handling, transportation, mixing of cattle from different sources, crowding and dusty environment increase the risk of BRSV infection in calves. Clinical signs related to BRSV are more pronounced during 7 to 10 days after a stressful event (Sacco *et al.*, 2014).

Infections related to BRSV are generally subclinical with an estimated incubation period of 2 to 5 days and mainly involve the upper respiratory tract. The main clinical signs related to BRSV infections are tachypnea, ocular serous secretion, dry muzzle, reduced activity, anorexia and fever (Sacco *et al.*, 2014).

The respiratory lesions in BRSV infection are more confined to the cranioventral lung tissues including cranial, middle and accessory lobes showing atelectatic, collapsed and deep red-purple rubbery areas of infection. Mucopurulent discharge is present in nasal meatus, trachea, bronchi and bronchioles in BRSV infection. Sometimes caudo-dorsal lobes are also involved which look distended due to emphysema and pale in color with the simultaneous presence of interlobular, lobular or subpleural lesions. Pulmonary lymph nodes including mediastinal and tracheobronchial lymph nodes enlarges due to infection response and look edematous or even hemorrhagic (Sacco *et al.*, 2014).

Microscopic lesions include Broncho-interstitial pneumonia, necrotizing bronchiolitis including necrosis of ciliated and non-ciliated bronchiolar epithelium, syncytia formation containing multinucleated syncytial cells, type II pneumocyte hyperplasia and alveolitis. Lumen of affected alveoli is filled with seroproteinaceous fluid, fibrin casts, cell debris, alveolar macrophages and sometimes neutrophils with thickening of alveolar septae and type II pneumocyte hyperplasia. In response to the viral necrotizing damage, the host healing efforts including fibroblast infiltration and neovascularization may result in bronchiolitis fibrosa obliterans due to fibrous polyps made into the airway lumen causing airway blockage (Sacco *et al.*, 2014).

The innate immune responses include the viral recognition by toll-like receptors (TLRs), retinoic acid–inducible gene I–like receptors and nucleotide-binding oligomerization domain–like receptors which are collectively called as pattern recognition receptors (PRRs) and binding of pathogen-associated molecular patterns (PAMPs) to these PRRs. Chemokines and cytokines are also involved on the inflammatory response after the attachment of PRRs with the viral PAMPs. These biochemicals activate the antigen-presenting cells such as dendritic cells, macrophages and the γδ T cells. Adaptive immune responses are caused by maternal antibodies, virus-specific antibodies and T-cells including CD4 and cytotoxic CD8 T cells (Sacco *et al.*, 2014).

Immunofluorescence and immunohistochemistry (IHC) of lung tissue are commonly used diagnostic tests to detect BRSV. Tests like polymerase chain reaction (PCR) and real-time reverse transcription PCR (RT-PCR) are also used to identify the simple presence of viral genome or to check the relative amount of BRSV mRNA of either F protein or nucleoprotein. One-step enzyme-linked immunosorbent assay is also helpful in detecting the BRSV. Postmortem examination, histopathology, IHC and RT-PCR are collectively more useful in detecting BRSV instead of viral isolation techniques (Sacco *et al.*, 2014).

Keeping the mind the controversial efficacy and the notable load of BRSV disease in cattle populations, huge efforts are required in order to develop more potent and targeted vaccines with suitable, strong and prolonged immune response (Sacco *et al.*, 2014).

Bovine Parainfluenza-3 Virus

Clinical signs related to Bovine parainfluenza-3 virus (BPIV-3) disease in calves are fever, nasal discharge and dry cough. The immunosuppression caused by BPIV-3 predisposes the calves for secondary infection by other

respiratory viruses and bacteria. Due to these reasons BPIV-3 plays an important role in the enzootic pneumonia in calves and bovine respiratory disease complex in feedlot cattle (Ellis, 2010).

Bovine Coronavirus (BoCV)

BoCV is a single-stranded, non-segmented RNA virus from family Coronaviridae which is responsible for severe diarrhea in newborn calves (CD), winter dysentery (WD) in adult cattle and respiratory tract infections contributing to the bovine respiratory disease complex (BRDC) in calves and feedlot cattle. BoCV is commonly detected by enzyme linked immunosorbent assay (ELISA) and reverse transcription-polymerase chain reaction (RT-PCR) in respiratory infections in cattle. The incidence of seroconversion of BoCV in feedlot cattle and its capacity to cause respiratory tract infections like BRD is still dubious. The sub-clinically infected animals are a potential source of infection for the non-infected animals in the herds (Hasoksuz *et al.*, 2002). Some studies show that the serologic evidence and consistently high prevalence of active BoCV infection related to its seroconversions is detected in a relatively large number of cattle with respiratory diseases proving that it may be an important cofactor in BRD (Martin *et al.*, 1998).

Pasteurella multocida is mainly responsible for the suppurative bronchopneumonia also called as lobular bronchopneumonia in young dairy calves. This type of bronchopneumonia is bilateral and cranioventral in nature which is initiated by the bronchial colonization of bacteria starting a suppurative bronchitis and then spreading along the airways causing deep respiratory lesions in lung lobules. The lesions in the affected lobes with mild interlobular septal edema looks variably from pink, pink-gray, dark red, red-gray or gray. Generally, pleuritis is not present in this type of pneumonia and it is characterized by purulent bronchitis, and bronchiectasis. *Arcanobacterium pyogenes* is associated with the chronic forms of this type of bronchopneumonia. Mainly *Mannheimia haemolytica* and to a lesser degree *Histophilus somni* are responsible for acute fibrinous pleuropneumonia/fibrinous bronchopneumonia/lobar pneumonia in stressed beef cattle (shipping fever) which is a firm, bilateral and cranioventral form of pneumonia. This type of pneumonia is characterized by extensive spread of the inflammation from the primary colonization site of bacteria in lobules to the whole cranioventral lobes. The severe invasive characters of LPS and LKT related to *Mannheimia haemolytica* are responsible for the quick and extensive spread to the lobules. Other related virulence factors like enzymes, oxygen radicals and inflammatory mediators are also helpful in this bacterial inflammatory spread. The interlobular septa are extensively distended due to yellow gelatinous fluid and coagulated fibrinous material, which gives the lung lobes a marbled appearance. Fibrinous pleuritis is also a characteristic feature of this type of pneumonia. Caseonecrotic bronchopneumonia is mainly caused due to *M. bovis* whose main colonization site is the ciliated respiratory tract epithelium. The chief characteristic of this type of pneumonia is perivascular cuffing by the lymphocytes. The main area containing the lesions is the anterior lobes of the lungs. The lesion consistency is firm and consolidated. Infection of the middle ear and joints can also be found with this kind of pneumonia. The viral pneumonia without the secondary bacterial infections is characterized by the broncho-interstitial pneumonia and is caused by BRSV, BHV-1 and PI-3, viruses. This type of pneumonia is characterized by bronchiolar epithelial damage, bronchiolar necrosis and hyperplasia of type-II pneumocyte cells and is seen in anterior parts of the lungs (Panciera and Confer, 2010).

Conclusion

BRD is a disease complex, which involves a number of causative factors including stress, primary viral infection and a concurrent bacterial infection. Environmental stress, inadequate ventilation, comingling of calves, over-crowding and poor nutrition are the major factors responsible for BRD. Failure of transfer of passive immunity in calves predisposes them to secondary bacterial infection. The current article provides an insight to scientists, researchers, veterinarians and progressive dairy farmers regarding various viral and bacterial pathogens associated with BRD.

Conflict of Interests

There is no conflict of interest.

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