Bacterial Pathogens Associated With Bovine Respiratory Disease Complex

Pneumonia is an inflammation of the tissues of the lungs that results from the response of the animal to an infectious agent, either a virus or bacteria, or in most cases both. Common viruses that can initiate pneumonia in cattle include: IBR (infectious bovinerhinotracheitis virus; a herpes virus), BRSV (bovine respiratory syncytial virus), PI3 (parainfluenza 3 virus), and BVD (bovine virus diarrhea virus). Often the virus infection will cause damage to the lung tissue and then bacteria will invade the compromised tissues. Lung damage from bacterial pneumonia, in the form of lesions, is generally the precipitating factor in BRDC related mortality. The four main bacterial pathogens involved in BRDC are opportunistic pathogens, normally residing in the respiratory tracts of healthy cattle, and becoming pathogenic when stress and secondary infection impairs immune function. Three of the main bacterial pathogens (Mannheimia haemolytica, *Pasturella multocida*, and *Histophilis somni*) frequently associated with BRDC are all generally susceptible to the same types of antibiotics. However, *Mycoplasma bovis* is a more genetically distinct bacterial pathogen involved in BRD. It lacks cell walls and is therefore not susceptible to some common types of antibiotics, like penicillin. The importance of knowing the bacteria involved in BRDC is that it can influence treatment options.

**Mannheimia haemolytica**

*Mannheimia haemolytica* (formerly named *Pasturella haemolytica*) is commonly isolated from the lungs of cattle with pneumonia. *Mannheimia haemolytica* is comprised of 12 capsular serotypes, with serotype A1 involved in most cases of pneumonia. Serotype A1 alone can cause pneumonia, but pneumonia symptoms are difficult to replicate without adding environmental stress or viral infection. The switch from commensal to pathogenic organism is considered density dependent, because virulence factors are stimulated when *M. haemolytica* is able to grow rapidly in the lung. One important virulence factor, leukotoxin, is excreted during the log phase of bacterial growth. Leukotoxin is thought to play a major role in lung injury due to its ability to damage white blood cells and elicit a vigorous inflammatory response.

**Pasturella multocida**

*Pasturella multocida* subsp. *multocida* ranks only below *Mannheimia haemolytica* in involvement in fatal cases of BRDC, but the involvement of *P. multocida* in BRDC has risen in recent years. The presence of *P. multocida* in the upper respiratory tract is not always associated with disease. It is not clear if commensal *P. multocida* converts to a pathogen in a density dependent manner, or if differences in the lung environment after viral infection favor the growth of more pathogenic isolates. *P. multocida* does generate a density dependent signal similar to *M. haemolytica*, but no toxins are known to be secreted from *P. multocida* involved in pneumonia. Other virulence factors, such molecules on the bacterial surface, may be important for *P. multocida* pathogenicity. *Pasturella multocida* is the only common BRDC pathogen that is zoonotic, or infectious to humans. *P. multocida* is generally transmitted to humans by animal bite, scratch, or lick.
**Histophilis somni**

*Histophilis somni* (formerly named *Haemophilus somnus*) is commonly isolated from the lungs of cattle with BRDC\(^2\). In addition to being associated with of BRDC, *H. somni* is involved in bovine infertility, abortion, septicemia, arthritis, myocarditis, and thrombotic meningencephalitis\(^17\). *H. somni* infections are characterized by inflammatory destruction of blood vessels\(^18\). *H. somni* virulence stems from molecules embedded on the bacterium’s cell surface. A primary virulence factor is lipooligosaccaride (LOS) which, along with other molecules on the cell surface, can mimic eukaryotic cell coatings, and may help hide the bacteria from the bovine immune system\(^17,19\). LOS can also damage endothelial cells and activate platelets, inducing vascular inflammation and coagulation\(^20,21\). Vascular inflammation is further exacerbated by the ability of *H. somni* to produce histamine\(^22\).

**Mycoplasma bovis**

For dairy calves, there are limited data on the prevalence of *M. bovis*. This bacterium has been the subject of considerable investigation; however, its primary role in bovine bacterial pneumonia is controversial\(^23\). *M. bovis* has been isolated from up to 45% of grossly and histologically normal bovine lungs\(^24\). The nasal prevalence of *M. bovis* in Californian dairy calves up to 8 months of age was 34% in herds with *M. bovis*-associated disease and 6% in nondiseased herds\(^25\). A longitudinal study showed that almost all calves in diseased herds became infected with *M. bovis*\(^26\). *M. bovis* is also associated with bovine mastitis, arthritis, and ear infections. *M. bovis* is the predominant cause of ear infections in cattle\(^27\), and infected animals may display ear droop, head tilt, and ear drainage due to infection of the middle ear\(^28\). Arthritis and lameness generally occur after prolonged *M. bovis* infections\(^29\). *M. bovis* should be suspected in cases of pneumonia that are unresponsive to antibiotic treatments, especially if accompanied by ear infection or arthritis\(^30\). Because mycoplasmas lack a cell wall, the β-lactam antimicrobials are not effective against these pathogens. Similarly, mycoplasmas do not synthesize folic acid and are therefore intrinsically resistant to sulfonamides. Mycoplasmas as a class are generally susceptible to drugs that interfere with protein (tetracyclines, macrolides, linosamides, and florfenicol) or DNA (fluoroquinolones) synthesis. However, *M. bovis* is resistant to erythromycin\(^31\). Unlike the other bacterial pathogens associated with BRDC, *M. bovis* is shed in the milk of infected cows. Feeding calves unpasteurized milk is thought to play a role in the transmission of *M. bovis*\(^32\).

**Treatment of Bacterial Pneumonia**

Early detection and treatment of BRD is a priority to quickly reduce the impact on infected bovine. Initial clinical signs include an elevated temperature, nasal and eye discharge, walking with a stiff gait, a crusty muzzle, salivation and mild diarrhea. Rapid shallow breathing and coughing are also early signs. Affected animals will often hang their heads and look lethargic. Their unwillingness to eat is closely tied to fever and depression. Evaluating calves for treatment using a screening system, such as the calf respiratory scoring chart which was developed at the University of Wisconsin, (http://www.vetmed.wisc.edu/dms/fapm/fapmtools/8calf/group_pen_respiratory_scoring_chart.pdf), and is based on rectal temperature, character of nasal discharge, eye or ear appearance and presence of coughing, has been recommended for dairy calves\(^33\).

Cases of bacterial pneumonia resulting from BRDC are typically treated with antibiotics, sometimes in conjunction with non-steroidal anti-inflammatory (NSAIDs). Success of antibiotic treatment is dependent on proper timing and dosage of drug administration and susceptibility of the bacterial pathogen(s) to the administered antibiotic. It is important to follow labeling instructions and veterinary guidelines as to the proper usage of antibiotics.
Vaccination Against Bacterial Pneumonia

USDA approved vaccines are available to help protect cattle against the four main bacterial pathogens involved in BRDC. The practice of vaccination against bacterial BRDC pathogens is common, but less so than vaccination against viral BRDC pathogens. However, the efficacy of vaccination in preventing or reducing the severity of BRDC is not well established. No decrease in treatments for respiratory disease was observed in young dairy calves vaccinated with a modified-live Mannheimia haemolytica and Pasteurella multocida vaccine. Therefore vaccination should be considered only one element of BRDC prevention, along with efforts to minimizing calf stress, colostrum feeding, and hygiene. Consult your veterinarian to determine a vaccination protocol that matches the needs of your herd with location-specific disease pressures.

Further reading and internet resources:
- Calf notes by Dr. Jim Quigley: English http://www.calfnotes.com
  Spanish/Español http://www.calfnotes.com/CNnotasterneros.htm
- Calf facts by Dr. Sam Leadley: English and Spanish/Español http://atticacows.com/
- University of Wisconsin Dairy Calf Clinical Information and Forms including respiratory scoring chart http://www.vetmed.wisc.edu/dms/fapm/fapmtools/calves.htm


34. USDA. Veterinary Biological Products. (United States Department of Agriculture Center for Veterinary Biologics, Ames, IA 2011).


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