

MYCOPLASMA BOVIS – AN EMERGING PATHOGEN IN RANCHED BISON

Introduction

Mycoplasma bovis (*M. bovis*) is a bacterial pathogen that recently became a major concern in the North American bison industry when ranchers began reporting high rates of *M. bovis* morbidity and mortality in their herds.

In bison, *M. bovis* seems to be a primary pathogen, causing disease in feedlots and in breeding-age cows on pasture, some with calves. Unlike feedlot animals, breeding herds are relatively closed to new additions. Calves in breeding herds are often disease-free but may perish due to lack of maternal care when they lose their dams (M. Woodbury, personal communication, April 4, 2013). Mature bulls suffer the same fate as affected cows. Mortality rates in adult bison have been as high as 25 percent, causing significant economic losses to producers (Woodbury and Windeyer, 2012).

Mycoplasma bovis disease in bison typically appears as pneumonia or pharyngitis with other lesions disseminated to various organ systems throughout the body (C. Windeyer, personal communication, September 12, 2013). Because *Mycoplasmas* do not produce toxins like other pneumonia-causing pathogens, affected animals remain alert early in the course of disease. However, when the herd moves, affected bison often trail behind due to exercise intolerance. Some producers have used this behavior as an early sign of *M. bovis* cases in their herds. The chronic nature of *Mycoplasma bovis* disease in bison eventually leads to emaciation and weakness. Affected bison are often euthanized to eliminate suffering when recovery is unlikely (Woodbury and Windeyer, 2012).

Stress may be a predisposing factor to *Mycoplasma bovis* disease in bison. Potential risk factors for pastured bison include introduction of new animals to the herd, nutrient stress from milk production, movement of bison among pastures, and excessive parasite loads



(C. Windeyer, personal communication, September 12, 2013). As forage quality declines in late summer and early fall, cows – particularly those that are nursing calves – may have lower resistance to *M. bovis*. Factors predisposing to disease at this time include hot weather, drought, and hardening of pasture grasses. (M. Woodbury, personal communication, April 4, 2013).

Epizootics of *Mycoplasma bovis* among ranched bison have occurred recently in multiple locations in Canada and the United States. It is unknown to what extent these outbreaks are influenced by geographic and environmental variables, or by differences in bacterial strains or disease resistance among bison herds. Because *Mycoplasma* species are prone to genetic reassortment, there could be emergent strains of *M. bovis* that are highly virulent for bison. Immunological strategies to protect bison from *Mycoplasma bovis* infection have yielded ambiguous results (M. Woodbury, personal communication, April 4, 2013).

Clinical Presentation

Mycoplasma bovis disease is a recent phenomenon within the North American ranched bison industry. Although anecdotal evidence for the emergence of *M. bovis* as a primary pathogen in bison has been accumulating, to date there are only four published reports in the scientific literature describing clinical manifestations of this disease (Dyer et al., 2008; Janardhan et al., 2010; Register et al., 2013a; Dyer et al., 2013). These reports are summarized in Table 1.

Table 1. Published case reports of Mycoplasma disease in North American bison herds.

Publication	Facility Type	Pathology	Age Class	Number Affected	Case Fatality
Dyer et al., 2008	Feedlot	Caseonecrotic pneumonia, Polyarthrititis, Laryngitis	Calves, Juveniles	20 dead, 7 sick	2.2%
Janardhan et al., 2010	Fenced State herd	Disseminated disease: Pneumonia, Pleuritis, Pericarditis, Polyarthrititis, Mastitis, Various other organs	Adults	53 total, 44 adult cows	27.3% Total 45.5% Adult cows
Register et al., 2013a	Rancher herd	Endometritis, Placentitis, Abortion, Caseonecrotic pneumonia, Fibrinous pleuritis, Caseonecrotic nephritis	Adults, Fetuses	15 adult cows	22.1%
Dyer et al., 2013	Undescribed herds	Caseonecrotic pharyngitis Liver abscesses	Calf, Adults	3	5% In one herd

Dyer et al. (2008) first reported *Mycoplasma bovis* in two feedlot bison found dead in North Dakota with severe, chronic, caseonecrotic pneumonia, polyarthrititis, and laryngitis. Twenty of 900 animals died before the first case was submitted to the laboratory. Lung lesions had prominent, well-defined areas of caseous necrosis and microscopic tissue-staining characteristics consistent with *M. bovis* patterns seen in cattle. Pathologic changes observed in necropsied bison were similar to chronic pneumonia and polyarthrititis syndrome (CPPS) in feedlot cattle caused by *M. bovis*.

Janardhan et al. (2010) investigated a disease outbreak of high morbidity and high mortality in a bison herd in Kansas. Affected bison were lethargic, arthritic, and in respiratory distress. Fifty-three of 194 animals died, including 40 of 88 adult cows. Necropsies of several bison revealed abscesses in lung and liver, disseminated microabscesses in other organs, as well as pleuritis, pericarditis, polyarthrititis, and mastitis. Lung and liver abscesses were large – up to 40 cm in diameter.

Register et al. (2013a) described a fatal *Mycoplasma bovis* infection in a bison cow and her aborted fetus from a herd with unusually high mortality associated with dystocia and abortion. During a 3.5-month period, 15 of 68 pregnant cows in the 80-head bison herd died during or after the birthing period. All affected bison were suspected of having *M. bovis*-related disease and most were in very poor condition at the time of death. The 15 calves from these cows were either stillborn or not found. Four of the affected cows were necropsied and all had caseonecrotic pleuropneumonia and endometrial necrosis. None of the herd's yearling bison or recently purchased bulls showed signs of disease.

Dyer et al. (2013) described a cluster of diagnostic cases in bison from the upper midwestern United States implicating *Mycoplasma bovis* as a pathogen associated with necrotic pharyngitis in bison. They isolated *M. bovis* from lesions of the pharynx and microscopically observed chronic caseonecrotic inflammation in the pharynxes. Distinctive histopathological features of the pharyngeal lesions favored causation by *M. bovis*, although a possible role for *Trueperella pyogenes* as a secondary bacterial invader could not be excluded. Additional testing did not reveal an underlying viral cause for the pharyngeal lesions. The authors concluded that *Mycoplasma bovis* should be considered a possible contributor to diphtheritic lesions and abscesses of the larynx and pharynx in bison.

There are multiple anecdotal accounts of bison losses among North American producers due to *Mycoplasma bovis* disease. In 2001, an outbreak of severe *M. bovis*-associated pneumonia with arthritis was diagnosed in a Saskatchewan bison herd (Woodbury and Windeyer, 2012). In 2007, Turner Enterprises, Inc. lost 380 breeding female bison in a Nebraska herd and 520 breeding females from a Montana herd (D. Hunter, personal communication, March 19, 2013). Since 2009, other producers from Montana to Oklahoma have suffered dramatic losses, including a rancher in South Dakota who lost 160 bison to *M. bovis* infection and successfully treated another 50 bison that were ill (D. Carter, personal communication, March 29, 2013). Bison producers in Alberta and Manitoba also lost breeding animals in 2009 to *M. bovis*, with no other pathogens found in hundreds of bison necropsies across the United States and Canada. The consensus from the International Bison Association meeting in Canada in 2012 was that *M. bovis* has become a primary pathogen

in ranched bison (D. Hunter, personal communication, March 19, 2013). Published and unpublished reports of *Mycoplasma bovis* disease in bison may represent the tip of the figurative iceberg for this disease in ranched bison herds (Woodbury and Windeyer, 2012).

Diagnosis

In cattle, rapid and accurate diagnosis of *Mycoplasma bovis* infection is compromised by the poor sensitivity and, in some cases, lack of specificity of available tests. Although research is underway, a bison-specific serologic test for *M. bovis* has not yet been developed (Register et al., 2013b). Moreover, subclinical *M. bovis* infections, intermittent shedding, uneven distribution of the bacterium in diseased tissue, and presence of *Mycoplasma* inhibitors in samples may complicate the diagnosis of this disease (Maunsell et al., 2011).

Register et al. (2013b) tested a collection of bison sera for *M. bovis*-specific antibody (IgG), mostly from animals with known history of infection or vaccination with *M. bovis*. They used commercially available kits, certified for use in cattle, as well as an ELISA developed in-house with bison *M. bovis* isolates as a source of antigen. Results demonstrated that ELISAs developed for cattle may be less suitable for identifying *M. bovis*-seropositive bison, particularly those with low to moderate levels of antibody. The ELISA performed best with capture antigen derived from bison isolates and when using a Protein G conjugate for detection of bison IgG rather than an anti-bovine IgG conjugate.

In cattle, immunohistochemistry (IHC) is the most diagnostically specific method to detect *Mycoplasma bovis* infection, whereas bacterial culture is a more sensitive method of detection (Caswell et al., 2010). In theory, tests that detect *M. bovis* antigen in cattle tissue should also work well in bison tissue (K. Register, personal communication, September 16, 2013). The main diagnostic advantage of IHC is that *M. bovis* antigen can be localized to specific areas of necrosis in the lung, suggesting a causal role for this pathogen in the development of lesions. In situ hybridization, which detects bacterial DNA in histologic sections, has similar advantages but is not widely available in diagnostic laboratories. Real-time polymerase chain reaction (PCR) systems with high sensitivity and specificity have also been developed for *Mycoplasma bovis* detection in clinical samples (Maunsell et al., 2011).

Clinical Case Definition

Animal scientists in Canada developed a broad case definition to assist in identifying disease of bison possibly caused by *Mycoplasma bovis* (Woodbury, 2012). Of interest, at the herd level, is



any unusually high incidence of disease or death affecting mature and/or young bison, with or without reduced fertility (high numbers of non-pregnant cows) or abortions. The following signs in an individual bison could indicate *Mycoplasma bovis* disease: reluctance to move, coughing, breathing difficulty, lethargy, exercise intolerance, isolation from the herd, and severe weight loss often resulting in death or need for euthanasia.

Necropsy findings indicative of *Mycoplasma bovis* disease in bison include poor nutritional condition accompanied by severe fibrinonecrotizing pneumonia, sometimes pleuropneumonia with prominent pulmonary sequestra. The infection is often widely disseminated, but locations of lesions are inconsistent and may include joints, endometrium, mammary gland, and various other organs. Lesions at distant sites are typified by areas of caseous necrosis and may grossly resemble bovine tuberculosis caused by *Mycobacterium bovis*. Diagnosis is confirmed by histopathologic lesions typical of *Mycoplasma bovis* infection in combination with the identification of the organism by IHC, PCR, or culture (Woodbury, 2012).

Reservoirs and Transmission Pathways

Although bacterial transmission through respiratory secretions is considered important in the epidemiology of *Mycoplasma bovis* infections (Caswell et al., 2010), there are few experimental data to support this view. Various direct and indirect routes of spread in cattle and bison are possible, including aerosols, nose-to-nose contact, or through feed, water, and fomites. *M. bovis* has been detected in the air of barns housing diseased calves, and calves have been infected experimentally by inhalation of aerosolized *M. bovis*. Fomite-mediated transmission of *Mycoplasma bovis* in respiratory secretions is also likely given that fomites can be important in the transmission of *M. bovis* mastitis (Maunsell et al., 2011).

Introduction of subclinically infected animals is thought to be the primary means by which *M. bovis*-free herds become infected (Maunsell et al., 2011). In Canada, it has been observed (anecdotally) that illnesses usually begin 6-8 weeks after new animals are brought in, and are confined either to the newly introduced bison or to the resident herd. Both groups are seldom affected. This observation suggests a role for naïvete in the course of clinical *Mycoplasma bovis* disease in bison (C. Windeyer, personal communication, September 12, 2013).



Once *Mycoplasma bovis* is present in a bison herd it can spread quickly. Shedding can range from intermittent in animals with no signs of disease, to heavy and persistent in clinically ill animals (Woodbury and Windeyer, 2012). Stressful events or conditions such as transshipment, entry into a feedlot, mixing of unfamiliar animals, and cold or hot weather are associated with increased rates of nasal shedding (Boothby et al., 1983). Shedding may be delayed, making it hard to pinpoint the source of *Mycoplasma bovis* in seemingly closed herds (Maunsell et al., 2011).

Environmental reservoirs of *M. bovis* are generally not regarded as important pathways for spreading infection (Caswell et al., 2010). However, research is needed to define the role of environmental persistence in *M. bovis* epidemiology (Maunsell et al., 2011). While *Mycoplasmas* are susceptible to drying and sunlight, *M. bovis* can survive for long periods in cool, damp environments. *M. bovis* has been shown to persist for months in recycled sand bedding and occurs in cooling ponds and dirt lots on dairies (Maunsell et al., 2011).

In the outbreak of *Mycoplasma bovis* in Kansas bison, no new animals had been introduced into the herd in the four years before the outbreak (Janardhan et al., 2010).

Although “a few elk” commingled with the bison, a cattle herd pastured adjacent to the affected bison herd was suspected as the source of infection. In the *M. bovis* outbreak among bison in the North Dakota feedlot, recovery of the bacterium from one nasal swab in the clinically ill group of bison suggested that it was shed by the nasal route. It is likely that additional clinically ill animals were shedding *M. bovis* into the environment and were a source of infection for herd mates (Dyer et al., 2008). The origin of *M. bovis* infection in these bison is unknown. An untested theory is that clinically healthy bison could carry strains of *M. bovis* that could later cause disease when other stress factors emerge (K. Register, personal communication, September 10, 2013). In light of reports on the severity of *Mycoplasma bovis* disease in bison, it is important for producers to adopt preventive measures to avoid *M. bovis* exposure and infection (Janardhan et al., 2010).

Treatment and Prevention

Hallmarks of antimicrobial therapy for *Mycoplasma* disease in cattle are chronicity and repeated relapses, especially among cases that on necropsy have lesions of caseonecrotic bronchopneumonia (Caswell et al., 2010). Beta-lactam antimicrobials are ineffective against *Mycoplasma* species because these pathogens lack a cell wall. *Mycoplasmas* also do not synthesize folic acid, making them resistant to sulfonamides. *Mycoplasmas* are generally susceptible to drugs that interfere with protein or DNA synthesis, although *M. bovis* is resistant to erythromycin (Maunsell et al., 2011).

Empirical evidence with bison has shown that treatment for *Mycoplasma bovis* infection is often promising at first, but animals commonly relapse and treatment must be sustained over several weeks to achieve any success. Bison with *M. bovis* arthritis likely respond very poorly to treatment, as do cattle (Maunsell et al., 2011), and those with *M. bovis* pneumonia frequently die or are euthanized for humane reasons despite treatment (Woodbury and Windeyer, 2012).

Although commercial and autogenous vaccines against *Mycoplasma bovis* have been developed that stimulate antibody production (in cattle), there is little evidence of their efficacy under field conditions. In some instances, *M. bovis* vaccines that appeared promising in challenge studies have increased the severity of disease when applied in field trials. Given the doubtful value of *Mycoplasma bovis* vaccines in cattle, these products are

not a recommended preventive strategy for *M. bovis* disease in bison (Woodbury and Windeyer, 2012).

The best way to prevent *Mycoplasma bovis* infections in ranched bison is to maintain a closed herd or to test and quarantine new animals before introducing them into the herd. In Canada, several outbreaks of *M. bovis* disease occurred after bison were reintroduced from feedlots to breeding herds or placed back on pasture. This practice is common in the bison industry, as the animals are typically fed through multiple seasons and years before slaughter. Revising this practice so that bison are moved only one way – to feedlots – could greatly reduce the risk of spreading *Mycoplasma bovis* and other pathogens to naïve herds (C. Windeyer, personal communication, September 12, 2013).

In theory, serologic testing could be used to identify uninfected bison herds from which to purchase replacement animals for cow-calf operations. However, there is no widely available serologic test for *M. bovis* that has been certified for use in bison, and the ELISA test for cattle that performs best in bison requires further evaluation before it can be fully endorsed for widespread use with bison sera (K. Register, personal communication, September 10, 2013). Purchased bison that have not been exposed to *M. bovis* should not be placed in seropositive herds as this practice places the introduced animals at risk for *Mycoplasma bovis* disease (Woodbury and Windeyer, 2012).

This same high level of biosecurity is impractical for bison in feedlot environments. Instead, management should focus on maximizing general respiratory health and immune function by minimizing handling, lowering stocking densities, and reducing other sources of stress (Woodbury and Windeyer, 2012). Sick animals should be segregated and other hygiene practices employed when treating bison. *Mycoplasma bovis* can persist in the environment but the bacterium is killed by chlorhexidine, chlorine, or iodine-based disinfectants. All implements and instruments used for treatment should be thoroughly disinfected (Maunsell et al., 2011).

Consequences for the Industry

Although the economic consequences of *Mycoplasma bovis* disease in bison cannot be accurately estimated at present, the costs are likely substantial based on recent empirical evidence of disease in commercial herds. Death and culling losses, reduced herd production, and

expenses for diagnosis, treatment, and control all contribute to the economic impact on ranchers and the industry. Because *M. bovis*-associated disease is chronic, costs-per-case are high relative to other pathogens. In addition to economic costs, there are important animal welfare consequences of *Mycoplasma bovis* infections, given that the disease is often long lasting and poorly responsive to treatment (Maunsell et al., 2011).

Future Directions

Mycoplasma bovis infection could be the most important emerging infectious disease issue faced by the North American commercial bison industry (Woodbury and Windeyer, 2012). Yet, because this disease is new to bison, it is poorly understood. Research is needed to establish the molecular and genetic basis for *M. bovis* infection in bison and to identify risk factors for the large outbreaks of severe *M. bovis*-associated pneumonia and arthritis that have plagued the industry. It is unknown whether there are differences in *Mycoplasma* resistance between bison herds and, since *M. bovis* is prone to reassortment, there could be emergent strains that are highly virulent for bison (M. Woodbury, personal communication, April 4, 2013).



Research is needed to develop practical, bison-specific diagnostic tests and effective treatment and prevention strategies to deal with the costly and harmful effects of *Mycoplasma bovis* epizootics (Woodbury and Windeyer, 2012). To date, immunological promotion strategies for *M. bovis* infections in bison have shown mixed results. Among cattle, vaccination in some cases has pre-sensitized animals, exacerbating clinical disease when they did become infected. It is unknown whether bison would respond similarly to vaccination (M. Woodbury, personal communication, September 13, 2013). Research is also needed to assess the economic efficiency of long-term treatment for *Mycoplasma bovis* infection; there have been no published studies that have critically evaluated the duration of therapy for *M. bovis*-associated disease (Maunsell et al., 2011).

In 2013, Canadian researchers launched an epidemiological study of *Mycoplasma bovis* disease in bison to explore some of these important topics.

Through a combination of laboratory and field research, and on-farm surveys, they will investigate the molecular and genetic basis for virulence of *M. bovis* in bison and will examine risk factors for infection among herds.

Basic questions to answer include:

- Is there a carrier state in which *Mycoplasma bovis* normally resides in the respiratory tract of bison;
- What role, if any, does pre-existing disease play in *M. bovis* epizootics among bison; and,
- Which traits of *M. bovis* and bison are keys to triggering illness, i.e. “is it the bison, the bug, or both?”

There are many unanswered questions about this disease – at the herd, animal, and molecular levels (M. Woodbury, personal communication, April 4, 2013).

In parallel with researchers in Canada, USDA:APHIS:VS is planning a national survey of the U.S. commercial bison industry that will take place in 2014. This survey will focus initially on general health and management practices within the industry and epidemiological risk factors for diseases and pathogens of concern, including *Mycoplasma bovis*. USDA will collaborate with Canada to develop the survey so that it complements Canada’s ongoing research on *M. bovis* disease in bison. This survey could lead to a more focused study of *M. bovis* or other bison health and management topics identified as important to the U.S. ranches bison industry.

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