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Integrating ecology with management to control wildlife brucellosis

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Summary

Bison (*Bison bison*) and elk (*Cervus elaphus*) in the greater Yellowstone ecosystem have long been infected with *Brucella abortus*. The continued culling of large numbers of Yellowstone bison to reduce the risk of brucellosis transmission to cattle could negatively affect long-term conservation. A desirable management objective is to reduce the level of *B. abortus* infection while conserving wildlife populations. Identifying the ecological factors that influence immune suppression and vulnerability to infection will help initiate effective control measures. Seasonal food restriction during pregnancy has the potential to limit resources available for immune defence and may be an important factor sustaining brucellosis in wild ungulate populations. Consequently, effective management practices will need to include a diverse range of integrated methods, which include maintaining separation of livestock and wildlife, managing habitat to reduce brucellosis transmission, and reducing disease prevalence in wildlife. The long-term success of these management practices will depend on sound science and support of the stakeholders involved.

Keywords

Bison – Brucellosis – Elk – Habitat – Management – Nutritional condition – Persistent pathogen – Pregnancy – Season – Yellowstone National Park.

Introduction

The rapid development of land by humans has reduced the amount of habitat available for wildlife (13). Much of the wildlife habitat that does remain is often fragmented or found within wildlife reserves, such as national parks. Loss of habitat to human development along the boundaries of these preserves has increased the proximity of humans, domestic animals, and wildlife to each other. Consequently, the risk of infectious disease spread between wildlife, livestock, and/or humans is a legitimate concern that is challenging for wildlife conservation along the boundaries of protected areas (39). This has long been the case with brucellosis management in bison (*Bison bison*) and elk (*Cervus elaphus*) in the greater Yellowstone ecosystem.

Brucellosis is a contagious disease, caused by the bacterium *Brucella abortus*, that can induce abortions or the birth of non-viable calves in livestock and wildlife (47). The bacterium is believed to have been introduced by European livestock to Yellowstone bison and elk before 1930 (36). In wildlife and cattle, infection typically occurs through contact with infectious reproductive tissues shed after abortions or live births (55). Though rare in the United States, human brucellosis can occur if bacteria are ingested or enter through the eyes or open wounds. *Brucella abortus* infection is rarely fatal in humans, with human-to-human transmission being insignificant (23). However, if not treated early, human brucellosis can cause recurring, severe, fever-like symptoms (62).

To minimise the effects on humans in the United States, a nationwide programme to eradicate brucellosis from cattle has been in place since 1934. The programme has successfully eliminated *B. abortus* from most of the United States, with the exception of free-ranging wildlife within the greater Yellowstone ecosystem (approximately 12 million acres in the states of Wyoming, Montana, and Idaho). Concerns over the risk of brucellosis transmission to cattle have led to decades of conflict regarding the management of bison and elk. The enduring debate over bison management has largely concentrated on the culling of animals that roam outside park boundaries during the winter. Therefore, a desirable objective is to reduce the prevalence of *B. abortus* infection while conserving wildlife populations.

The long-term success of bison conservation depends on the availability of low-elevation winter habitat outside the park. 'Habitat' has traditionally been used to describe the spatial

surroundings of an animal during a stated time, but this definition fails to capture the seasonally variable resources that influence fitness (i.e. survival and reproductive output) (37). For large mammalian herbivores, the availability of forage to meet these fitness needs is a key element of habitat quality. To reduce the risk of brucellosis transmission from bison to cattle, bison access to ranges outside the park is restricted. Within the park, deep snow reduces foraging opportunities during late winter and early spring. Understanding how seasonal food restriction influences infection and transmission of brucellosis in wild ungulates may be important for developing effective management practices.

Brucellosis control measures will be more effective if the mechanisms sustaining infection in wildlife populations are better understood. The maintenance of brucellosis in Yellowstone bison may be linked to periods of nutritional stress and reduced immune function, both seasonally and across host life stages (57). Yellowstone bison are seasonal breeders with moderate synchrony in spring calving (34). This reproductive schedule restricts *B. abortus* transmission to mainly late gestation near parturition when there is an influx of vulnerable hosts (e.g. naïve newborns) into a nutritionally stressed population. Simultaneous investment in immune defence and reproduction may not be an option if both food and internal resources (i.e. protein and energy reserves) are limited. The endemicity of brucellosis in Yellowstone bison may be a consequence of vulnerability in young animals and limited food availability during reproductive seasons.

The focus of this review is to advance our understanding of how brucellosis is maintained within wild ungulates and to use this information to improve disease management practices in the Greater Yellowstone Area. First, the author discusses the seasonal factors influencing the nutritional condition of wild ungulates and how these factors may increase susceptibility to persistent pathogens, such as *B. abortus*. Next, how this information can be used to develop brucellosis management practices specific to wild ungulates in the greater Yellowstone ecosystem will be reviewed.

Seasonal food restriction and disease susceptibility in wild ungulates

Wild ungulates are hosts to several zoonotic intracellular pathogens, which are commonly associated with livestock and humans. Many of these pathogens are able to establish persistent infections within their hosts and have been notoriously difficult to eradicate from humans, domestic animals, and infected wildlife (16, 23, 48). In wild ungulates, these disease agents can induce abortions in pregnant females and may influence population dynamics and compromise the conservation of threatened populations (33, 43). Effective tools and strategies for managing or eradicating persistent diseases in wildlife are largely unavailable because we have only a rudimentary understanding of disease dynamics in wildlife populations.

In mammals, cell-mediated immune responses, which provide protection from intracellular pathogens, are naturally suppressed during pregnancy (14, 63). Consequently, the success of many intracellular pathogens is linked to modifications of the cell-mediated immune mechanisms that protect the developing fetus (5, 20, 29, 35). The brucellae are capable of modulating cellular functions. This enables the bacteria to survive within host cells (macrophages) and await the opportunity to infect the reproductive tract during pregnancy (11, 54). The inability of the host to clear or control persistent pathogens can result in reactivation of infection, especially during periods of immune suppression (7). Thus, chronic infection of wild ungulate populations may result from the effectiveness of these persistence strategies during periods when immune defences are physiologically down-regulated.

Wild ungulates often experience periods of nutritional restriction, which can influence the maintenance and transmission of infectious disease (1). Poor nutrition alters virtually every aspect of the immune response, including vulnerability to attack and reactivation of chronic infections (32). The nutritional condition of mammalian herbivores is driven by seasonal forage availability and quality. Early plant growth stages generally have high nutrition in terms of energy and protein (61). Since immune defence is fuelled by protein and energy (8), periods of food restriction may increase susceptibility to persistent pathogens. At these times, intracellular pathogens, which exploit their hosts during pregnancy, may face less resistance from immune defences if hosts are in poor nutritional condition (4).

Various aspects of the immune system are condition dependent, with immune responsiveness positively associated with nutritional condition and the availability of dietary nutrients (19, 21, 28, 66). For example, a negative correlation has been observed between prevalence of bovine tuberculosis in African buffalo (*Syncerus caffer*) and body condition (10). In temperate and northern regions, the dietary protein and energy needed to fuel immune responses are largely reduced for wild ruminants in the months before the emergence of spring vegetation (42). At this time, ungulates have depleted energy reserves (fat) which can inhibit an effective immune response when combined with

low levels of dietary protein (25, 38). Protein scarcity seems to affect cellular immunity to a much larger extent than it affects antibody-mediated immunity (9). Some intracellular pathogens (e.g. members of the *Brucella, Mycobacterium* and *Salmonella* genera) have evolved virulence mechanisms that can modulate the host's cellular immune system, thereby increasing their ability to establish persistent infections (46, 54). During periods of food restriction, this infection strategy may be particularly effective in malnourished hosts (17).

For pregnant bison, late gestation is a protein- and energy-demanding state, as increasing demands of fetal development coincide with food restriction. Yellowstone bison and elk are typically in negative energy balance during winter when endogenous reserves (fat and body protein) are used to meet energy requirements until spring green-up (18). For bison, calving is timed to coincide with the emergence of highly nutritious spring forage, which meets lactational demands and increases calf survival (50). However, the synchronisation of parturition with the availability of food in late spring means that pregnant bison are in a state of reduced body condition during late winter and early spring when food is limited and reproductive demands of late gestation are high. The seasonal reduction in protein and energy can create a bottleneck that constrains immune defences (8) and may open a transmission and infection window for *B. abortus* (57). Additionally, newborns and reproductively immature bison, which are closely associated with pregnant females, may be prone to *B. abortus* exposure during the transmission period (58).

The endemicity of brucellosis infection might be influenced by the fact that food restriction occurs during periods of increased reproductive demands. In Yellowstone bison, seasonal food restriction was found to reduce nutritional condition during late gestation, with the probability of active brucellosis infection being highest for bison in below-average condition (57). Based on these findings, it is hypothesised that variation in winter severity may influence annual brucellosis transmission, with more bison unable to resist *B. abortus* infection during years with severe or prolonged winters. Such heterogeneity in *B. abortus* transmission may help explain the observed fluctuations in bison seroprevalence over past decades.

Balancing conservation with effective disease management

The high seroprevalence (40% to 60%) of brucellosis in Yellowstone bison might imply that they are an infection source for Yellowstone elk. However, recent data suggest that transmission between bison and elk is rare (45). The peak bison calving period, when the most bacteria are expected to be shed, occurs approximately one month earlier for bison than for elk, with little overlap in distribution during this time period. Elk that mingle with bison in the Madison headwaters area in Yellowstone have much lower seroprevalence rates for brucellosis (3%) than elk that mingle with other elk at feedgrounds in Wyoming (22%) (45, 52).

The role of elk in the maintenance of brucellosis in the northern portion of the greater Yellowstone ecosystem has traditionally been viewed as less important than that of bison. Unlike most bison, female elk segregate themselves from other herd members while giving birth (31). Elk birth sites are dispersed and well cleaned, with the likelihood of other elk encountering infectious birth tissues being low. But transmission risk may be higher during late winter and early spring when elk form large aggregations on low-elevation winter ranges, where abortions under these conditions could expose many susceptible elk to infectious material (26). These conditions facilitate elk-to-elk transmission and may be sustaining brucellosis in elk populations away from feedgrounds (15)

Although brucellosis-infected elk have been responsible for disease transmission to cattle (3, 27), Yellowstone bison have long been the primary focus of brucellosis management in the northern portion of the Greater Yellowstone Area. In some years, large numbers of migrating bison are captured and tested for brucellosis, with seropositive animals being shipped to slaughter. The combination of severe winter conditions and high population density encourages bison movement to low-elevation ranges outside Yellowstone (22), where they are not tolerated by state governments and members of the local community because of the risk of transmitting brucellosis to cattle. Approximately 3,200 Yellowstone bison were shipped to domestic slaughter facilities between 2001 and 2010, with 899 shipped during 2006 and 1,434 shipped during 2008. These large-scale bison removals are not random because female bison and their recent offspring (i.e. male and female calves and yearlings) are the demographic culled as they move onto low-elevation winter ranges outside the park. As a result, these culling practices have contributed to a skewed sex ratio in favour of male bison and have created gaps in the population's age structure. This reduces productivity and could, over time, reduce the potential of Yellowstone bison to respond to future population challenges (64).

The limited ability of diagnostic tests to accurately identify active *B. abortus* infection has led to disease management practices that are not aligned with wildlife conservation. Bison infection status has been determined with antibody tests, which cannot distinguish active from inactive infection and have little correlation with long-term protection. Because *B. abortus* antibodies are long lived (47), test-and-

slaughter practices may be removing a large proportion of older bison that have developed some level of immune protection (e.g. cell-mediated immunity), which is not measured on serological tests. These recovered animals may provide protection to the overall population through the effect of herd immunity (30), thereby reducing the spread of disease. As a management tool, serological tests can be misleading if there is no understanding of how they relate to active infection.

During 2008, over 400 Yellowstone bison were sampled at slaughter facilities in Montana and Idaho to better understand the association between active infection (e.g. isolation of *B. abortus*), antibody levels, and bison age (58). The data suggested that *B. abortus* in bison behaves much like an endemic disease, with infection occurring primarily in young animals and recovery increasing with age. Active infection increased rapidly in young bison and peaked during the age of first pregnancy. The high seroprevalence observed in reproductively immature bison suggests that active *B. abortus* infection begins early in life and probably results from close associations with infectious, pregnant females. Bison in early reproductive ages represent a large population demographic and may play a greater role in maintaining brucellosis infection than do older animals, a large proportion of which have recovered from *B. abortus* infection acquired earlier in life. These findings have been used to develop a diagnostic tool that will help managers identify potentially infectious bison, which will improve brucellosis reduction efforts (58). The tool allows managers to estimate probabilities of active infection in live bison based on serum antibody levels and bison age (estimated via incisor eruption patterns). Managers can use this information during different phases of brucellosis vaccination programmes. In the early phase, when seroprevalence is high, few animals are removed for disease management purposes. After seroprevalence declines in young bison (i.e. the reproductively immature age class) through vaccination, managers can focus on removing bison that have a high probability of active infection, which is expected to be a small proportion of animals. This targeted approach removes high-risk individuals and increases herd immunity through vaccination, while promoting bison conservation without large-scale culling (58).

Brucellosis reduction

The inability of some wildlife hosts to recover from *B. abortus* infection leads to chronic infection and the continual presence of disease reservoirs in the population. Since *B. abortus* is known to establish long-term infection, we can never be certain that seropositive individuals have completely recovered from infection by clearing all bacteria. We can also expect infected wildlife populations to remain infected without active disease reduction efforts. Traditional test-and-slaughter programmes have been effective for managing diseased livestock, but these practices may not be effective, realistic, socially acceptable, or ethical for wildlife (6, 24, 40, 64). As a management tool, culling is rarely appropriate for controlling wildlife diseases and may increase disease prevalence under certain conditions (2, 12, 65).

Deciding on appropriate disease management practices for wildlife frequently leads to disagreements between state and federal agencies, the concerned public, and stakeholders (e.g. Native American tribes, livestock producers, and conservation groups). Disease eradication is usually the option preferred by livestock producers (51), but this may not be possible for persistent diseases in wildlife. Managing the risk of disease transmission from infected wildlife to livestock typically involves practices that maintain spatial separation. Though spatial separation will help protect livestock from infected wildlife, it does not reduce disease prevalence in wild ungulates and requires a continuous investment in management and surveillance efforts.

Wildlife vaccination has been proposed as an alternative to culling and has been successful in some situations in reducing infectious disease (49, 56). However, delivering vaccines to free-ranging wildlife poses significant challenges (44). Additionally, vaccines that generate long-lived cellular responses for protection against intracellular disease agents have not provided consistent protection (53). Because immune responses against intracellular pathogens have high nutritional costs, the efficacy of vaccines tested under experimental conditions may be reduced in wild ungulates in natural conditions. In Yellowstone bison, protein and fat metabolism were identified as important factors influencing the intensity of *B. abortus* infection and cell-mediated immune responses (interferon-γ production) in yearling females following vaccination (57). The nutritional resources needed to induce protective immune responses following vaccination may not be available during late gestation for wild ungulates. Further research is needed to compare vaccine efficacy under experimental and natural conditions to assess how food restriction during pregnancy influences the effectiveness of vaccines against *B. abortus* infection.

Long-term monitoring will be an essential component of any brucellosis reduction programme. Until diagnostic tests are improved, seroprevalence is expected to be the primary metric by which the level of brucellosis infection is determined. Therefore, monitoring the effectiveness of vaccination will require a surveillance programme which recognises the limitations of serological tests in determining the effectiveness of vaccination. From a management perspective, it will be important to distinguish whether a short-term reduction in disease prevalence resulted from management suppression efforts or environmental factors

that improve host resistance during the critical period (e.g. mild winters, food availability). If infection levels spike despite consistent disease reduction efforts, public support for these efforts may be short-lived. In the greater Yellowstone ecosystem, it is not yet possible to eradicate *B. abortus* in wild ungulates, but it is possible to do more than manage the transmission risk to cattle. Management practices can be refined to reduce the prevalence of infection in a manner that is better aligned with long-term bison conservation. Until improved tools are developed (such as efficacious vaccines, realistic delivery methods, accurate diagnostic tests, and effective monitoring methods [60]), reducing the level of infection may be the strategy most supported by the management agencies, stakeholders and concerned public.

Conclusion

The focus of this review has been to advance our understanding of how brucellosis is maintained within wild ungulates and to use this information to improve disease management practices. Identifying the ecological factors that influence immune suppression and vulnerability to infection will help initiate effective control measures. Seasonal food restriction during pregnancy has the potential to limit resources available for immune defence and may be an important factor sustaining brucellosis in wild ungulates. The high prevalence of infection observed in reproductively immature bison suggests that primiparous bison may be the primary reservoir sustaining brucellosis in the Yellowstone population. Therefore, it would be beneficial to focus disease reduction efforts, such as vaccination, on young female bison, with efforts (e.g. booster vaccination) continuing into adulthood (41, 59). Antibodies produced against *B. abortus* decline slowly, so the level of infection in older animals is probably overestimated. Consequently, serological tests can be misleading if there is an inadequate understanding of how they relate to active infection. Therefore, combining vaccination with the selective removal of potentially infectious individuals will advance brucellosis management in a manner that is more aligned with bison conservation.

The periodic large-scale culling of test-positive bison has not been effective at reducing brucellosis prevalence and, if applied more broadly, this practice can negatively affect the long-term conservation of wild ungulates. Although wildlife vaccination has potential to reduce disease prevalence, efficacious vaccines that induce long-lived cellular responses are lacking. Nutritional factors, such as seasonal food restriction and loss of body reserves, may play an important role in the effectiveness of wildlife vaccination programmes. Research is needed to link within-host processes (e.g. nutrition) with the induction of protective immune responses against *B. abortus* infection. Protective immune responses induced through vaccination may be limited if vaccines are delivered to undernourished animals.

Brucellosis risk management in the greater Yellowstone ecosystem is one of the great challenges facing large mammal conservation in North America. Effective management practices will need to include a diverse range of integrated methods, which include maintaining separation of livestock and wildlife, managing habitat to reduce brucellosis transmission, and reducing disease prevalence in wildlife. The long-term success of these management practices will depend on sound science and support from the stakeholders involved. Otherwise, efforts to balance brucellosis management with wildlife conservation are unlikely to be successful.

Concilier écologie et gestion dans la lutte contre la brucellose chez les animaux sauvages

J.J. Treanor

Résumé
L'infection à *Brucella abortus* est présente depuis longtemps chez le bison (*Bison bison*) et le cerf élaphe (*Cervus elaphus*) au sein de l'écosystème du Grand Yellowstone. L'abattage continu et massif des bisons du Yellowstone dans le but de réduire le risque de transmission aux bovins de la brucellose peut avoir des effets néfastes sur la survie à long terme de l'espèce. L'objectif d'une gestion harmonieuse consiste à réduire le niveau d'infection à *B. abortus,* tout en protégeant les populations d'animaux sauvages. La connaissance des facteurs écologiques qui contribuent aux dysfonctionnements de l'immunité et à la sensibilité vis-à-vis de l'infection permettra de mettre en place des mesures de lutte efficaces. La diminution saisonnière de l'alimentation pendant la période de gestation diminue les ressources nécessaires à la défense immunitaire et pourrait être un facteur important de la persistance de la brucellose chez les ongulés sauvages. En conséquence, une gestion efficace doit associer des pratiques correspondant à diverses méthodes intégrées, notamment la séparation des animaux d'élevage et sauvages, la gestion de l'habitat afin de réduire les risques de transmission de la brucellose et la réduction de la prévalence de la maladie chez les animaux sauvages. L'application raisonnée de principes scientifiques et le soutien actif des parties prenantes concernées sont des conditions nécessaires à la réussite durable de ces pratiques de gestion.

Mots-clés
Agent pathogène persistant – Bison – Brucellose – Cerf élaphe – État nutritionnel – Gestation – Gestion – Habitat – Parc national du Yellowstone – Saison.

Integración de la ecología y la gestión para combatir la brucelosis en la fauna salvaje

J.J. Treanor

Resumen
Hace tiempo que el bisonte (*Bison bison*) y el ciervo común (*Cervus elaphus*) vienen sufriendo infecciones por *Brucella abortus* en el ecosistema del Gran Yellowstone. El continuo sacrificio sanitario de un gran número de bisontes de Yellowstone para reducir el riesgo de transmisión al ganado vacuno podría influir negativamente en la conservación a largo plazo de ese bovino salvaje. Un objetivo de gestión deseable es el de reducir el nivel de infecciones por *B. abortus* y a la vez conservar las poblaciones de animales salvajes. Para poner en marcha medidas eficaces de control resultará útil determinar los factores ecológicos que influyen en la inmunosupresión y la vulnerabilidad a la infección. La escasez de alimentos que se produce durante la estación reproductiva puede limitar los recursos disponibles para la defensa inmunitaria y constituir así un factor importante en el mantenimiento de la brucelosis en las poblaciones de ungulados salvajes. Por consiguiente, a la hora de instaurar prácticas eficaces de gestión será preciso incluir una panoplia de métodos integrados, como mantener la separación entre ganado y fauna salvaje, gestionar los hábitats para contener

la transmisión de la brucelosis y reducir la prevalencia de la enfermedad en los animales salvajes. El éxito a largo plazo de tales prácticas de gestión dependerá de su sólido fundamento científico y del apoyo de todas las partes interesadas.

Palabras clave
Bisonte – Brucelosis – Ciervo común – Condición nutricional – Embarazo – Estación – Gestión – Hábitat – Parque Nacional de Yellowstone – Patógeno persistente.

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